

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Parts 310, 347, and 352

[Docket Nos. 78N–0021 and 78N–021P]

RIN 0910–AA01

Skin Protectant Drug Products for Over-the-Counter Human Use; Final Monograph

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is issuing a final rule in the form of a final monograph establishing conditions under which over-the-counter (OTC) skin protectant drug products are generally recognized as safe and effective and not misbranded as part of the ongoing review of OTC drug products conducted by FDA. The final monograph includes OTC skin protectant drug products for minor cuts, scrapes, burns, chapped skin and lips, poison ivy, poison oak, poison sumac, and insect bites. FDA is issuing this final rule after considering public comments on the agency's proposed regulation, which was issued in the form of a tentative final monograph, and all new data and information on skin protectant drug products for these specific uses that have come to the agency's attention. This final rule amends the regulation that lists nonmonograph active ingredients by adding those OTC skin protectant ingredients that have been found to be not generally recognized as safe and effective. This final rule also lifts the stay of 21 CFR part 352 (published at 66 FR 67485, December 31, 2001) to amend the final monograph

for OTC sunscreen drug products to include sunscreen-skin protectant combination drug products, and then stays § 347.20(d) (21 CFR 347.20(d)) and part 352 until further notice in the **Federal Register**.

DATES: *Effective Date:* This rule is effective [*insert date 12 months after date of publication in the* **Federal Register**].

Compliance Dates: The compliance date for products subject to parts 310 and 347 (21 CFR parts 310 and 347) with annual sales less than \$25,000 is [*insert date 24 months after date of publication in the* **Federal Register**]. The compliance date for all other products subject to parts 310 and 347 is [*insert date 12 months after date of publication in the* **Federal Register**]. The compliance date for combination products containing skin protectant and sunscreen active ingredients in § 347.20(d) and for all products subject to part 352 is stayed until further notice.

Comment Date: Submit written or electronic comments on specific labeling items discussed in section X of the **SUPPLEMENTARY INFORMATION** section of this document by [*insert date 90 days after date of publication in the* **Federal Register**].

ADDRESSES: Submit written comments to the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Submit electronic comments to <http://www.fda.gov/dockets/ecomments>.

FOR FURTHER INFORMATION CONTACT: Gerald M. Rachanow, Center for Drug Evaluation and Research (HFD-560), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-827-2222.

SUPPLEMENTARY INFORMATION:

I. Background

In the **Federal Register** of August 4, 1978 (43 FR 34628), FDA published an advance notice of proposed rulemaking to establish a monograph for OTC skin protectant drug products, together with the recommendations of the Advisory Review Panel on OTC Topical Analgesic, Antirheumatic, Otic, Burn, and Sunburn Prevention and Treatment Drug Products (the Panel), which was the advisory review panel responsible for evaluating data on the active ingredients in this drug class (§ 330.10(a)(6) (21 CFR 330.10(a)(6))).

In the **Federal Register** of February 15, 1983 (48 FR 6820), FDA published the proposed regulation for OTC skin protectant drug products in the form of a tentative final monograph (TFM). In the **Federal Register** of October 3, 1989 (54 FR 40808), the agency published a document to amend the TFM to include OTC drug products for poison ivy, oak, and sumac and for the treatment and/or neutralization of insect bites. This final rule completes the TFMs published on February 15, 1983, and October 3, 1989, amends the final monograph for OTC skin protectant drug products used as astringents in part 347 published on October 21, 1993 (58 FR 54458), and incorporates the name change (“witch hazel”) published in the **Federal Register** of June 3, 1994 (59 FR 28767).

In the **Federal Register** of May 10, 1993 (58 FR 27636), the agency issued a final rule establishing that certain active ingredients, including some skin protectant active ingredients, in OTC drug products are not generally recognized as safe and effective or are misbranded. These skin protectant ingredients are listed in § 310.545(a)(18). This final rule adds several ingredients to that section.

On or after 12 months after date of publication in the **Federal Register**, and 24 months after date of publication in the **Federal Register**, for products

with annual sales less than \$25,000, except combination products containing skin protectant and sunscreen active ingredients, and for combination products containing skin protectant and sunscreen active ingredients, no OTC drug product that is subject to this final rule and that contains a nonmonograph condition may be initially introduced or initially delivered for introduction into interstate commerce unless it is the subject of an approved new drug application or abbreviated new drug application. Further, any OTC drug product subject to this final rule that is repackaged or relabeled after the effective dates of the final rule must be in compliance with the monographs regardless of the date the product was initially introduced or initially delivered for introduction into interstate commerce. Manufacturers are encouraged to comply voluntarily as soon as possible.

All “OTC Volumes” cited throughout this document refer to information on public display in the Dockets Management Branch (see **ADDRESSES**).

II. The Agency’s Conclusions on the Comments

(Comment 1) One comment stated its continuing position that OTC drug monographs are interpretive, as opposed to substantive, regulations.

The agency addressed this issue and reaffirms its conclusions stated in paragraphs 85 through 91 of the preamble to the procedures for classification of OTC drug products (37 FR 9464 at 9471 to 9472, May 11, 1972); in paragraph 3 of the preamble to the TFM for OTC antacid drug products (38 FR 31260, November 12, 1973); and in paragraph 1 of section I of the preamble to the TFM in the present proceeding (48 FR 6820 at 6821).

(Comment 2) One comment requested that the definition of “skin protectant” be reworded to add a primary effect of skin protectants, i.e., temporary relief of the effects of harmful or annoying stimuli and to include

the word “product”. The agency agrees and is revising the definition of “skin protectant” in § 347.3(d).

(Comment 3) Four comments opposed the agency’s “exclusivity policy,” which limits the indications used in OTC drug product labeling to the “specific words and phrases” approved by FDA in a final OTC drug monograph.

After these comments were submitted, the agency published a final rule in the **Federal Register** of May 1, 1986 (51 FR 16258) changing its labeling policy (§ 330.1(c)(2) (21 CFR 330.1(c)(2))) for stating the indications for use of OTC drug products. That policy was revised and discussed in the **Federal Register** of March 17, 1999 (64 FR 13254 at 13270 to 13271, and 13294). The final rule in this document is subject to that new labeling policy.

(Comment 4) Three comments disagreed with the agency’s position of prohibiting cosmetic claims from appearing in any portion of the labeling that is required by an OTC drug monograph and the agency’s view that this type of labeling could be misleading (see 48 FR 6820 at 6823). One comment noted its support for the distinction made by the agency between “drug” and “cosmetic” claims for the same ingredient. Two comments cited current agency regulations in § 701.3(d) (21 CFR 701.3(d)) regarding the combined label declarations of active drug ingredients and cosmetic ingredients and requested that cosmetic indications be allowed to be stated in a manner that is not false or misleading, without regard to their position on the label.

The agency has revised its labeling requirements for OTC drug products by adding § 201.66 (21 CFR 201.66) and amending § 701.3(d) since stating its position on drug-cosmetic labeling in the TFM. Section 701.3(d) now requires separate listing of the active drug ingredients and the cosmetic ingredients where a cosmetic product is also an OTC drug product. FDA does not review

and approve cosmetic terminology in OTC drug monographs. Under the new OTC drug product labeling format in § 201.66, the “Drug Facts” area of a product’s labeling only contains the indication(s) for the drug part of the product. Thus, manufacturers are not allowed to commingle drug and cosmetic claims within this specific area of the labeling. However, there are no specific restrictions on commingled information outside of the “Drug Facts” area of a product’s labeling. The agency’s position is that if commingled drug and cosmetic labeling information is confusing or misleading, the product’s labeling may be misleading within the meaning of the Federal Food, Drug, and Cosmetic Act (the act) and the product misbranded under sections 502(a) or 602(a) of the act (21 U.S.C. 352(a) or 362(a)). The agency will review the labeling of affected products on a case-by-case basis.

(Comment 5) Several comments suggested that limiting the statement of identity to one term (“skin protectant”) is too restrictive, requested other equally descriptive appropriate terms, and asked for distinct statements of identity for each indication proposed in the monograph, e.g., “minor cut protectant.”

The agency does not find it necessary to have distinct statements of identity for each use of a skin protectant drug product. The statement of identity is intended to provide information on the “general pharmacological category(ies) of the drug or the principal intended action(s) of the drug” (see § 201.61(b) (21 CFR 201.61(b))). This position is consistent with the statement of identity proposed by the agency as “external analgesic” for all drug products that provide relief of pain and itching caused by a number of conditions (48 FR 5852 at 5868, February 8, 1983) and as “analgesic (pain reliever)” for all

drug products that relieve pain due to various conditions (53 FR 46204 at 46211, November 16, 1988).

The agency concurs with one comment's suggestion of adding the dosage form to the statement of identity, i.e., "skin protectant (dosage form)." The *United States Pharmacopeia (USP)* lists a number of dosage forms that might be used for OTC topical drug products (Ref. 1). From a marketplace survey (Refs. 2, 3, and 4), the agency finds that the most widely used dosage forms for OTC skin protectant drug products are lotions, creams, ointments, and gels. The examples of dosage forms listed in the statement of identity in § 347.50(a) of this final monograph are not all inclusive and depend on products' historical marketing as skin protectants.

(Comment 6) One comment questioned the agency's statement that the term "soothes" is a cosmetic claim in the context of skin protectant products (48 FR 6820 at 6828).

The agency considers claims such as "temporarily protects" and "helps relieve" to be more informative than "soothes" in conveying to consumers that a drug product provides therapeutic action. The term "soothes" may appear elsewhere in the product's labeling.

(Comment 7) Several comments contended that the indications proposed were too restrictive and omitted indications recommended by the Panel. The comments suggested additional labeling claims.

The agency agrees with some of the comments' suggestions for the indications in § 347.50(b)(2). While the agency wishes to emphasize the "protectant" function of these ingredients, they may also help provide some relief for chapped or cracked skin and lips. Therefore, the agency is allowing manufacturers to add, at their option, the words "and helps relieve" after the

word “protects” in the indications in § 347.50(b)(2). The agency also agrees that the words “cold” and “wind” are informative to consumers, and possibly easier to understand than the word “windburned.” Accordingly, the agency has made this revision in an optional labeling statement.

The agency considers other suggested claims to be better represented in the agency’s proposed indications.

The agency is deleting “sunburn” from the indication proposed in § 347.50(b)(1) because the agency has reexamined the data and determined that they do not support a “protection of sunburn” claim for these ingredients. The “sunburn” claim proposed in the TFM originated from the Panel when it recommended the use of “skin protectant active ingredients for symptoms of dryness: ‘For symptoms of chapping, peeling or scaling’ (optional, any or all of the following) ‘due to minor burns, sunburn, windburn, scrapes, abrasions, or cracked lips’” (see 43 FR 34628 at 34648). The Panel also recommended that the ingredients allantoin, cocoa butter, dimethicone, glycerin, petrolatum, and shark liver oil be included in the monograph as active ingredients for symptoms of dryness. Of these ingredients, petrolatum was the only one that the Panel discussed effectiveness for sunburn (43 FR 34628 at 34639). The Panel stated that “the use of petrolatum as an emollient has been well accepted for dry skin conditions, especially with flaking skin such as sunburn, and chapping” (43 FR 34628 at 34639).

The Panel’s claim was revised in the TFM to a shortened “drug” claim that stated: “For the temporary protection of minor cuts, scrapes, burns, and sunburn” (see 48 FR 6820 at 6832). The agency did not include peeling or scaling claims in the TFM (48 FR 6820 at 6828). The Panel’s reference to symptoms of dryness was not included in the TFM because the agency

considers the use of skin protectants for dryness to be a cosmetic claim. The agency has now determined that it should not have included the “sunburn” claim in the TFM because the only context in which the Panel discussed it was cosmetic in nature.

The agency is also concerned that skin protectants may inappropriately be used for “sunburn” because the data indicate that it is not desirable to apply a skin protectant to sunburn that has just occurred. As the Panel noted, when petrolatum is applied to sunburn, evaporation is curtailed (43 FR 34628 at 34639). The agency is concerned that application of skin protectants, such as petrolatum and the other ingredients for which the Panel recommended a dryness claim for sunburn, to sunburn that has just occurred would occlude the area and prevent evaporation from occurring or significantly reduce evaporation. Thus, there are no data in the administrative record for this rulemaking to support a “protection of sunburn” claim for these ingredients. The agency would consider including such a claim for these ingredients, however, if adequate supporting data are provided.

The agency has determined that insufficient data were submitted to include the words “to allow healing to begin” and to include uses for heat rash, burning feet, and foot discomfort in § 347.50(b)(3). The agency concludes that the expanded “uses” section in this final monograph provides manufacturers an adequate number of options for labeling OTC skin protectant drug products.

(Comment 8) One comment mentioned that no wound healing claim or Category I labeling was provided for three skin protectant ingredients: Allantoin, live yeast cell derivative (LYCD), and zinc acetate.

The Panel classified these ingredients as Category III skin protectants for wound-healing based on the lack of effectiveness data (43 FR 34628 at 34644 through 34647). Insufficient data were submitted for LYCD (see section II. comment 25 of this document) and no additional data were submitted for allantoin or zinc acetate to support a “wound healing” use.

(Comment 9) One comment requested that compound benzoin tincture be included as a Category I topical skin protectant. The comment mentioned the conclusion of the Advisory Review Panel on OTC Cold, Cough, Allergy, Bronchodilator, and Antiasthmatic Drug Products (Cough-Cold Panel) that compound benzoin tincture was safe for use in boiling water as a steam inhalant for expectorant purposes (41 FR 38312 at 38360, September 9, 1976). The comment also cited the recommendation of the Advisory Review Panel on OTC Dentifrice and Dental Care Drug Products (Dental Panel) that compound benzoin tincture was safe and effective for use as an oral mucosal protectant (47 FR 22712 at 22746 and 22747, May 25, 1982). The comment cited acceptance of compound benzoin tincture in several pharmacopeias, experience over decades of use, and the low incidence of adverse reactions or significant side effects in the published literature. The comment cited several skin protectant uses from well-established references or current product labeling: “* * * to small cuts and to intact skin under occlusive plasters and bandages” (Ref. 5), “* * * ulcers, bedsores, cracked nipples, and fissures of the lips and anus” (Ref. 6), and “apply to the skin under adhesive dressings, to treat skin fissures and bedsores, to reduce skin sensitivity to adhesive plasters, and to prevent skin irritation in ischemic areas” (Ref. 7).

Compound benzoin tincture is included in the *USP* as a fixed formulation containing 10 percent benzoin, 2 percent aloe, 8 percent storax, 4 percent tolu

balsam, and 74 to 80 percent ethanol (Ref. 8). The agency finds that use as a steam inhalant for expectorant purposes evaluated by the Cough-Cold Panel (41 FR 38312 at 38360) has little relevance to use as a skin protectant. Although the agency acknowledges that standard references (Refs. 5 and 6) and literature articles describe numerous uses for compound benzoin tincture, no data from controlled clinical studies were provided.

Gosselin et al. (Ref. 9) indicated that the alcohol in benzoin tincture would be responsible for major toxic effects if ingested. The Dental Panel discussed literature reports of three cases of irritation and hypersensitivity resulting from topical use of benzoin tincture (47 FR 22712 at 22746 and 22747). In addition, the published literature contains numerous other reports of allergic contact dermatitis and sensitivity attributed to compound benzoin tincture and benzoin tincture. Cullen, Tonkin, and May (Ref. 10) stated that the literature was replete with reports of cutaneous sensitivity to compound benzoin tincture and its components, citing reports following local application. Rademaker and Kirby (Ref. 11) reported two cases of bullous contact dermatitis to a skin adhesive spray and mentioned that Fisher (Ref. 12) recommends that benzoin no longer be used as a skin adhesive. Marks and Rainey (Ref. 13) and James, White, and Yanklowitz (Ref. 14) reported other cases of allergic contact dermatitis. Sixteen cases resulted when benzoin was applied to prevent friction blisters. Other authors report contact dermatitis from benzoin used as an ingredient in greasepaint makeup (Ref. 15) and as an antioxidant in food additives (Ref. 16). In addition, benzoin provokes pemphigus erythematosus (Ref. 17), complicates management of venous leg ulcers (Ref. 18), and adversely affects wound healing after circumcision in children (Ref. 19).

Based on these reports of adverse events and the availability of other monograph skin protectant ingredients, the agency concludes that compound benzoin tincture is not safe for use as a general OTC skin protectant ingredient and would be inappropriate for many of the uses included in this final monograph.

(Comment 10) One comment requested that camphorated metacresol be included as an active ingredient in the final monograph for OTC skin protectant drug products, as long as the amount of metacresol did not exceed 1.5 percent (by weight) and the amount of camphor did not exceed 3 percent. Noting that phenol (0.5 to 1.5 percent) and camphor (0.1 to 3 percent) were proposed Category I ingredients in the TFM for OTC external analgesic drug products (48 FR 5852 at 5867, February 8, 1983) and citing an agency letter (Ref. 20) agreeing that metacresol was less toxic than phenol, the comment contended that there should be no safety concern about products containing camphor and metacresol in these concentrations.

Because information has not been provided to demonstrate a skin protectant effect, camphorated metacresol is not included in this final monograph.

(Comment 11) One manufacturer submitted data and information (Refs. 21 and 22) to FDA's Miscellaneous External Panel in response to the call-for-data notice published in the **Federal Register** of November 16, 1973 (38 FR 31697). The data were for a drug product containing water-soluble chlorophyllins in an ointment and a solution dosage form with a label indication "to promote healing and to relieve itching and discomfort of minor wounds, burns, surface ulcers, cuts, abrasions and skin irritations."

The Miscellaneous External Panel was disbanded before reviewing these submissions. Subsequently, because the product label contained a claim for wound healing and products with this claim had previously been included in the skin protectant rulemaking, the agency placed the submissions in the skin protectant rulemaking as a comment to the February 15, 1983, TFM, and the manufacturer submitted a more recent study on effectiveness for wound healing (Ref. 23).

The Dental Panel evaluated water-soluble chlorophyllins as oral wound healing agents in its report on OTC oral mucosal injury drug products (44 FR 63270, November 2, 1979) and concluded that water-soluble chlorophyllins were safe but that there were insufficient data available to permit final classification of effectiveness for OTC use as an oral wound healing agent (44 FR 63270 at 63286). The agency accepted the Dental Panel's classification in the TFM for OTC oral mucosal injury drug products (48 FR 33984 at 33991, July 26, 1983). No additional data were submitted and, in the final rule (51 FR 26112, July 18, 1986), the agency included water soluble chlorophyllins in the list of nonmonograph ingredients in 21 CFR 310.534.

The agency has reviewed the manufacturer's submissions (Refs. 21, 22, and 23). One submission (Ref. 21) contained information on various kinds of wounds that were treated with water-soluble chlorophyllins by health-care professionals. None were self-treatment conditions. Another (Ref. 22) contained translations of three foreign articles reporting laboratory and animal studies on water-soluble chlorophyllins that contain background information but do not support general recognition of safety and effectiveness in humans. A research report (Ref. 23) did not assess OTC uses, lacked subject and placebo

controls, and questioned whether the observed effects were due to the products or the manner of caring for the wounds.

The agency concludes that the data submitted do not support effectiveness of water-soluble chlorophyllins for promoting wound healing for conditions treated with OTC skin protectant drug products.

(Comment 12) Cod liver oil was not categorized by the Panel for use as an OTC skin protectant because it was not included among the labeled ingredients in marketed products submitted to the Panel for review. In evaluating cod liver oil for use in diaper rash drug products, the agency considered the long history of clinical use as a skin protectant ingredient (55 FR 25204 at 25213, June 20, 1990).

In the rulemaking for OTC anorectal drug products, the Advisory Review Panel on OTC Hemorrhoidal Drug Products (Hemorrhoidal Panel) classified cod liver oil as Category I for use as an anorectal protectant and recommended a maximum daily dose of 10,000 I.U. (International Units equivalent to USP Units) for vitamin A and 400 I.U. for vitamin D (cholecalciferol) per 24 hours (45 FR 35576 at 35630, May 27, 1980). The Hemorrhoidal Panel stated that an extensive review of the literature on cod liver oil revealed no adverse effects when applied topically as a protectant and concluded that the effectiveness of cod liver oil, as a protectant, is due to its bland and soothing effect associated with its oily nature. In the TFM (53 FR 30756 at 30767, August 15, 1988) and final monograph (55 FR 31776 at 31780, August 3, 1990) for OTC anorectal drug products, the agency affirmed the Hemorrhoidal Panel's Category I classification and specified that cod liver oil may be used only in combination with one to three other protectant active ingredients.

The agency has surveyed the marketplace and determined that cod liver oil is marketed only in combination with other ingredients in several products with skin protectant claims (Refs. 3 and 24). One product contains 12.5 percent (Ref. 24), but in most cases the cod liver oil concentration is not provided.

Therefore, the agency is including cod liver oil as an active ingredient in skin protectant drug products in accord with § 347.20(a)(1) and (a)(2), only in combination with certain other skin protectant active ingredients, within the concentrations (5 to 13.56 percent) specified in § 347.10(e), provided that the product is labeled so that the amount of the product that is used in a 24-hour period represents a quantity that does not exceed 400 USP Units of vitamin D and 10,000 USP Units of vitamin A.

(Comment 13) In the notice of proposed rulemaking (54 FR 40808 at 40810), the agency stated that it was necessary to have publicly available chemical information for colloidal oatmeal. One manufacturer submitted a proposed standard for colloidal oatmeal, which it stated was patterned after standards for starch and psyllium (Ref. 25). The agency sent this information to the U.S. Pharmacopeial Convention (USPC) (Ref. 26). Compendial standards were proposed in the Pharmacopeial Forum of January and February 1992 (Ref. 27) and a final *USP* monograph became effective on November 15, 1992 (Ref. 28).

(Comment 14) One comment requested that colloidal oatmeal be included in the skin protectant monograph as a safe and effective ingredient for the claim: “For prompt temporary relief of itchy, sore, sensitive skin due to rashes, eczema/psoriasis, hemorrhoidal and genital irritations, diaper rash, chicken pox, prickly heat, hives, poison ivy/oak, and sunburn.” The comment cited references (Refs. 29 through 33) to support this claim.

The agency previously discussed poison ivy/oak claims in comment 1 of the skin protectant poison ivy, oak, and sumac notice of proposed rulemaking (54 FR 40808 at 40809 to 40811). The agency has determined the additional references cited by the comment show that colloidal oatmeal can provide temporary skin protection and relieve minor irritation and itching due to a number of conditions. Further, the agency has no adverse reaction reports on file for colloidal oatmeal. Thus, the agency is expanding the indications for colloidal oatmeal in § 347.50(b)(4) in this final monograph. In addition, manufacturers can opt to select one or more of the “due to” conditions to list in the product’s labeling. However, since no data were submitted using colloidal oatmeal for chicken pox, sunburn, or hives, these indications are nonmonograph. The agency will discuss a “prickly heat” claim in the skin protectant diaper rash drug products final rule.

(Comment 15) Two comments noted that the agency’s proposed directions in § 347.50 (54 FR 40808 at 40818) for the use of colloidal oatmeal as a soak in a tub do not allow for the range of use concentrations or dosage forms that have been reported in the clinical literature and requested that FDA specify a use concentration range. The comment stated that colloidal oatmeal is unusual in comparison to other barrier skin protectants because it is often intended for dispersion in water and is formulated in a variety of other dosage forms.

One comment summarized and calculated the colloidal oatmeal concentrations used in baths (Refs. 32 and 34 through 41). The comment noted that the most common concentration ranges of colloidal oatmeal are from 0.007 to 10 percent in use but added that colloidal oatmeal is present in commercial

products from 1 to 100 percent. Another comment recommended changing the proposed directions in § 347.50(d)(2) from one “cupful” to “up to a cupful.”

The agency has reviewed the recommended concentrations of colloidal oatmeal reported in the literature and reference texts (Refs. 4, 29 through 32, 34 through 45, 47, 48, and 49) and has considered the range of concentrations for colloidal oatmeal used in bath additive products and in other dosage forms. Products containing colloidal oatmeal have been formulated in the following dosage forms: Lotion (1 and 10 percent colloidal oatmeal), cleansing cream (8 percent colloidal oatmeal), shampoo (5 percent colloidal oatmeal), and cleansing bars (30, 50, and 51 percent colloidal oatmeal) (Refs. 4, 46, and 47). The agency has calculated the approximate minimum and maximum concentrations of colloidal oatmeal that have been used as follows: For regular colloidal oatmeal, a range of 0.023 to 0.625 percent when used as a tub bath soak (Refs. 29, 34 through 38, and 44), a range of 0.24 to 1.2 percent when used as a foot bath soak (Refs. 30, 31, and 34), a range of 0.24 to 15 percent in aqueous solution when used in a wet pack (Refs. 30, 31, 32, 34, and 45), and a range of 3.75 to 15 percent in aqueous solution when used as a topical lotion (Refs. 30, 32, and 34); for oilated colloidal oatmeal, a range of 0.003 to 0.03 percent when used as a tub bath soak (Refs. 35 and 39 through 43).

With regard to dosage forms, the agency agrees with the comment that colloidal oatmeal as a skin protectant does not need to be dosage-form specific and can be used in a variety of “barrier type” topical dosage forms, except for “cleanser type” topical dosage forms, for which the agency has no data to support use as a skin protectant. Therefore, based on the additional information that has been submitted, the agency is revising the directions for use in § 347.50(d)(2) in this final monograph.

(Comment 16) One comment requested that colloidal oatmeal be included in the skin protectant monograph for the claim: “For prompt temporary relief of itchy, sore, sensitive skin due to * * * hemorrhoidal and genital irritations * * *.” The comment provided reports recommending use of colloidal oatmeal baths and creams for rectal itching and other conditions in the genital area (Refs. 50 through 54).

Claims for itching in the genital area (e.g., pruritus vulvae) are included in the rulemaking for OTC external analgesic drug products. A comment to that rulemaking (Ref. 55) specifically requested a claim for colloidal oatmeal for “prompt temporary relief of itchy, sore, sensitive skin due to rashes, eczema/psoriasis, hemorrhoidal and genital irritations, diaper rash, chicken pox, prickly heat, hives, poison ivy/oak, and sunburn.” Therefore, the agency will address this comment in the final rule for OTC external analgesic drug products.

The agency concludes that the comment’s requested claims for relief of rectal itching and hemorrhoids are similar to the indication (21 CFR 346.50(b)(1)) for OTC anorectal drug products that include protectant active ingredients under 21 CFR 346.14, and to the definition of a protectant drug under 21 CFR 346.3(i) as a drug that provides a physical barrier, forming a protective coating over skin or mucous membranes. Since colloidal oatmeal was not reviewed during any stage of the rulemaking for OTC anorectal drug products, interested parties should provide necessary information to demonstrate that colloidal oatmeal meets the standards of an OTC anorectal protectant active ingredient and petition the agency to include colloidal oatmeal in the final monograph for OTC anorectal drug products (Ref. 56).

(Comment 17) One comment requested that colloidal oatmeal be allowed to be combined with other Category I skin protectants for the treatment of minor irritation and itching caused by insect bites and poisonous plants. The comment cited reports using an oilated colloidal oatmeal bath additive to help treat various dermatoses.

The agency has reviewed the cited studies (Refs. 34, 43, 57, 58, and 59), and finds that these reports support the combination of colloidal oatmeal with mineral oil to treat the irritation, itching, and dryness of various dry skin dermatoses. The agency is including the combination of colloidal oatmeal and mineral oil in new § 347.20(a)(4) for the uses included in new § 347.50(b)(7) of this final monograph. Nevertheless, poison ivy, oak, and sumac are not exclusively dry skin dermatoses; they are characterized by a phase of weeping, oozing exudation. The studies cited by the comment fail to demonstrate the value of adding an additional skin protectant (an oilating component) for the treatment of these conditions in the exudative phase, and also fail to specify how many of the cases of contact dermatitis were due to poisonous plants. In addition, only one case of insect bite was identified in the studies. The agency concludes that the data are insufficient to support the combination of colloidal oatmeal with other skin protectants to treat insect bites and poison ivy, oak, and sumac.

(Comment 18) One comment responded to the agency's request in the skin protectant poison ivy, oak, and sumac notice of proposed rulemaking (54 FR 40808 at 40810) to provide information and directions to support the use of colloidal oatmeal on children under 2 years of age. The comment stated that most barrier type skin protectant active ingredients have not been restricted to any age group and submitted reports of use of colloidal oatmeal in infants

(Refs. 34, 45, 50, 51, and 57). The comment added that the Miscellaneous External Panel had evaluated colloidal oatmeal and placed it in Category I for relief of itching claims with no age restrictions (Ref. 61).

The agency has reviewed the reports submitted by the comment, which described the effective use of colloidal oatmeal on infants and children from 2 months to 18 years of age for various dermatoses associated with dry skin. No adverse effects were reported. The Miscellaneous External Panel (Ref. 61) at its twenty-third meeting concluded that colloidal oatmeal, at all concentrations, is safe and effective for “the symptomatic relief and treatment of itching.” Based on the Miscellaneous External Panel’s evaluation and the references provided by the comment, the agency is including colloidal oatmeal in the final monograph for use on infants and children under 2 years of age in the same concentrations, dosage forms, and directions for use for adults.

(Comment 19) One comment noted that in the skin protectant poison ivy, oak, and sumac notice of proposed rulemaking the agency proposed (in § 347.50(c)(9)) a specific warning for colloidal oatmeal: “Take special care to avoid slipping when getting into and out of the tub” (54 FR 40808 at 40818). The comment agreed that a warning against slipping is proper and appropriate, but contended that the agency’s warning is unnecessarily longer than the warning on its labels, “Take special care to avoid slipping.” Furthermore, the comment contended, the reference to entering and leaving the tub may lessen the consumer’s perception of need for care during bathing or when bathing a child.

The agency notes that a number of authors have expressed concerns about slipping in the bath tub with oil baths in general, and with colloidal oatmeal baths in particular (Refs. 29, 40, 44, 48, 54, and 62). Two authors (Refs. 29

and 48) recommended use of a mat to reduce the possibility of slipping.

Accordingly, the agency has revised the warning, which appears in § 347.50(c)(5) of the final monograph, to read: “When using this product [bullet] to avoid slipping, use mat in tub or shower.”

(Comment 20) One comment objected to the highly specific directions for colloidal oatmeal the agency proposed in § 347.50(d)(2) of the skin protectant poison ivy, oak, and sumac notice of proposed rulemaking (54 FR 40808 at 40818). The comment requested that FDA modify the directions for use to allow for other concentrations and to address the use of other dosage forms, such as ointments, lotions, and cleansing bars. The comment objected to a specified frequency of use (“once or twice daily”) because absorption of active agent seems unlikely to occur.

The agency has reviewed the literature and agrees with the comment that other directions may also provide safe and effective use concentrations. Since a bathtub, foot bath, sitz bath, or infant bath can be used to soak and a compress or wet dressing can be applied as a soak, the agency is including all of these forms of a “soak” in the final monograph. Colloidal oatmeal can also be formulated in other topical products intended for direct application (e.g., ointment, lotion), and the monograph provides directions for these products.

Frequent and prolonged exposure to water may have a drying effect. Authors have different views on recommended frequency and duration of bathing (Refs. 37, 48, and 63 through 67) depending on the condition. The Miscellaneous External Panel noted that bathing can dry the skin out and exacerbate some conditions (Ref. 68). Given the variety of conditions for which colloidal oatmeal preparations may be used, the agency agrees with the

comment and is not specifying a frequency of use in the directions but is providing for a warning statement in § 347.50(c)(7) to fully inform consumers.

(Comment 21) One comment inquired whether two high-molecular weight dimethylpolysiloxanes, designated as SF96–350 and SF96–1000, were acceptable active ingredients for skin protectant use. The comment included general safety and toxicity information on silicone products, and stated that dimethicone, a proposed Category I skin protectant ingredient, belongs to the same chemical family as the dimethylpolysiloxanes.

In the notice of proposed rulemaking for OTC skin protectant diaper rash drug products, the agency stated that silicone is a general term, but it is often used to describe dimethicone (55 FR 25204 at 25218). The agency did not classify silicone per se because there are various silicone compounds and because the agency considered dimethicone, the only silicone ingredient for which data were submitted.

The agency notes that the information provided by the comment summarizes the results of chronic and acute toxicity studies and irritation studies for specific classes of silicones. However, no specific information was provided for the individual dimethylpolysiloxanes SF96–350 and SF96–1000. In addition, no information was provided to describe the chemical structure of these dimethylpolysiloxanes. The agency concludes that the data provided are inadequate to support general recognition of the safety and effectiveness of these ingredients for OTC skin protectant use in this final monograph.

(Comment 22) In the TFM for OTC skin protectant drug products, the agency discussed a submission on 2 percent glycerin and stated that the skin protectant final monograph would not be issued until these data were reviewed by the agency and interested persons provided an opportunity to comment on

an agency proposal (48 FR 6820 at 6823). The submission (Ref. 69) contained data on the use of glycerin for the indications of dry skin, minor skin irritation, skin protectant, and chapping and included a double-blind study.

The agency has reviewed the data and determined that the study was inadequately controlled and failed to demonstrate that 2, 10, or 18 percent glycerin is effective for the indication “helps prevent and temporarily protects chafed, chapped, cracked, or windburned skin and lips,” as proposed by the agency for 20 to 45 percent glycerin in the TFM for OTC skin protectant drug products (48 FR 6820 at 6832). The agency’s detailed comments and evaluation of the data are on file in the Dockets Management Branch (Ref. 70). The agency concludes that glycerin at concentrations other than 20 to 45 percent is nonmonograph for use in OTC skin protectant drug products.

(Comment 23) One comment requested the agency to reopen the administrative record to include the ingredient “hard fat,” as described in the “National Formulary” (NF) (Ref. 71), as a Category I skin protectant.

In the **Federal Register** of December 19, 1991 (56 FR 65873), the agency agreed with the petition that it would be appropriate to reopen the administrative record and include data and information on “hard fat” in the rulemaking for OTC skin protectant drug products. The agency stated that, based on its action in the rulemaking for OTC anorectal drug products (55 FR 31776), hard fat would be classified as a monograph ingredient in the final skin protectant monograph. Since no adverse comments on hard fat were received in response to this reopening of the administrative record, the agency is including hard fat in § 347.10 at concentrations of 50 to 100 percent as a single active ingredient. Hard fat is also allowed in permitted combinations in § 347.20(a)(1), (a)(2), (b), (c), and (d) of this final monograph. Products

containing hard fat may be labeled for the indications in § 347.50(b)(1), (b)(2)(i), and (b)(2)(ii) and should bear the warnings in § 347.50(c)(1) through (c)(4) and the directions in § 347.50(d)(1). In a future issue of the **Federal Register**, the agency will address claims for hard fat in OTC skin protectant cold sore/fever blister drug products (see proposed § 347.50(b)(2)(ii), 55 FR 3362 at 3370).

(Comment 24) One comment requested that lanolin be categorized as an active ingredient in the skin protectant monograph for use as a single ingredient or in combination, as permitted by the monograph. In support of lanolin's safety and effectiveness as a skin emollient, the comment cited animal and human test data submitted to the Miscellaneous External Panel (Ref. 72), Kligman, Grove, and Studemayer (Ref. 73), and the Advisory Review Panel on OTC Ophthalmic Drug Products' (Ophthalmic Panel) Category I classification of lanolin as an ocular emollient for the treatment of conditions involving ocular membranes (43 FR 30002 at 30044 and 30045, May 6, 1980).

The agency has considered lanolin as a protectant or emollient active ingredient in several OTC drug rulemakings. In the TFM for OTC skin protectant diaper rash drug products (55 FR 25204 at 25218 to 25219), the agency determined that the data submitted supported the use of 15.5 percent lanolin as a skin protectant active ingredient only in combination with other skin protectant active ingredients for the treatment and prevention of diaper rash.

In the final rule for OTC ophthalmic drug products (53 FR 7076 at 7090, March 4, 1988), lanolin and anhydrous lanolin were included as monograph conditions at a 1 to 10 percent concentration in combination with one or more oleaginous emollients included in the monograph. In the final rule for OTC

anorectal drug products (55 FR 31776 at 31780), lanolin was included as a monograph protectant active ingredient at concentrations of 50 percent and above as a single ingredient or between 12.5 and 50 percent in combinations.

The agency has surveyed the marketplace (Refs. 3, 74, 75, and 76), and found that lanolin is being marketed as a skin protectant both as a single ingredient and in combination with other ingredients. The concentration in two single ingredient products is 37 and 50 percent. In almost all cases, the concentration of the lanolin in the combination products is not provided. Based on the agency's market survey and its previous actions in the rulemakings for OTC diaper rash, anorectal, and ophthalmic drug products, the agency is including lanolin in the final skin protectant drug products monograph as a single ingredient and in combination with certain other skin protectant active ingredients, depending on the labeled use of the product. The use concentration included in the final monograph is 12.5 to 50 percent in accord with the concentration of marketed single ingredient skin protectant drug products and the concentration used in anorectal protectant combination drug products. The use concentration of 15.5 percent proposed in § 347.10(o) for OTC diaper rash skin protectant drug products (55 FR 25204 at 25232) will be addressed in the final rule for those drug products.

(Comment 25) One comment submitted data (Refs. 77 through 89), including two clinical studies by Kaplan (Refs. 77, 78, 80, 81, and 84), in support of reclassifying LYCD from Category III to Category I as a wound healing aid. The first Kaplan study (Ref. 77) has been published (Ref. 90). The comment also submitted data included earlier in the rulemaking for OTC anorectal drug products and transcripts of meetings of the Hemorrhoidal Panel (Ref. 87).

The ingredient LYCD was reviewed by both the Hemorrhoidal Panel and the Topical Analgesic Panel. Neither panel found LYCD to be effective. The agency determined that the data were inadequate to support the use of LYCD in the final rule for OTC anorectal drug products (58 FR 46746, September 2, 1993).

The agency has reviewed the wound healing studies (Refs. 77, 78, 80, 81, and 84) submitted to this rulemaking for OTC skin protectant drug products and determined that the studies are inadequate to include LYCD as a wound healing aid in this final monograph. The agency's detailed comments and evaluations of the nonconfidential data are on file in the Dockets Management Branch (Refs. 91 and 92).

The agency also informed the company that additional information is needed on the chemical and physical characterization of LYCD before a final classification can be made and suggested the company provide information to establish a compendial monograph for the ingredient (Ref. 93). The company submitted information, both nonconfidential (Refs. 88 and 89) and confidential, but it also was not adequate. The agency's detailed comments on the information are on file in the Dockets Management Branch (Refs. 94 and 95).

(Comment 26) The agency has included in the rulemaking for OTC skin protectant drug products several submissions (Refs. 96, 97, and 98) for drug products containing mineral oil that were originally submitted to the Miscellaneous External Panel for review. One submission (Ref. 96) did not contain any data on mineral oil as an individual ingredient and the other submissions (Refs. 97 and 98) were discussed in the TFM for OTC skin protectant diaper rash drug products (55 FR 25204 at 25220 to 25221). The

agency concluded that the ingredient's physical properties were sufficient, along with the Category I findings of two other panels (Hemorrhoidal and Ophthalmic Panels), to support the effectiveness of mineral oil in § 347.10(p) of the skin protectant diaper rash TFM (55 FR 25204 at 25232) for diaper rash claims proposed in § 347.50(b)(5). In this final monograph for OTC skin protectant drug products, mineral oil in the first concentration listed in § 347.10(l) (50 to 100 percent) may be labeled for the claims listed in § 347.50(b)(1) and (b)(2). In addition, mineral oil in the second concentration listed in § 347.10(1) (30 to 35 percent) when combined with colloidal oatmeal may be labeled for the claims listed in § 347.50(b)(7).

(Comment 27) One comment urged FDA to consider a single statement of identity for the ingredient petrolatum because of its multi-purpose uses in OTC drug products. The comment suggested the term “protectant.”

Petrolatum is generally recognized as safe and effective in two other OTC drug final monographs: Ophthalmic (part 349 (21 CFR part 349)) and anorectal (21 CFR part 346). The statement of identity for ophthalmic use is “lubricant” or “emollient (lubricant) eye ointment” (see § 349.65(a)).

The agency previously considered a related issue in the proposed rulemaking for OTC anorectal drug products (see comment 39, 53 FR 30756 at 30771) and determined that a comment's suggested statement of identity (topical protectant and lubricant) did not make it clear that such a product could be used anorectally and thus did not fully satisfy the requirements of § 201.61(b). The agency believes that the same is true of the currently suggested statement of identity “protectant.” Thus, the agency is not adopting a single statement of identity for the ingredient petrolatum and is using “skin

protectant” as the statement of identity for drug products containing petrolatum included in this final monograph (part 347).

(Comment 28) One comment argued that petrolatum should be exempt from the “directions for use” proposed in § 347.50(d), citing petrolatum’s long history of consumer use, efficacy, and safety and contending that petrolatum meets the requirements for such exemption under § 201.116 (21 CFR 201.116).

The agency disagrees. Section 201.116 allows for exemption from section 502(f)(1) of the act which requires adequate directions for use, if adequate directions for common uses are known to the ordinary individual. While some individuals may know that petrolatum may be applied as needed, the agency believes that not all people who use this drug would know that it can be applied on an as needed basis. Therefore, the agency is requiring the standard direction in § 347.50(d)(1) for products that contain petrolatum.

(Comment 29) One comment contended that petrolatum should be exempt from the warnings proposed in the TFM (48 FR 6820 at 6832 to 6833). The comment argued that sufficient evidence to exempt these warnings is provided by the universal use of petrolatum over many decades for a wide variety of topical indications, the clinical and marketing experience over this long period of extensive and universal use, the Panel conclusion that “large amounts of petrolatum are essentially nontoxic when ingested * * *” (43 FR 34628 at 34639), the results of a long-term chronic feeding study by Oser et al. (Ref. 99) as demonstrating safety on ingestion, and the fact that petrolatum is regulated as an approved direct food additive (under § 172.880 (21 CFR 172.880)) and is listed in the Food Chemicals Codex (Ref. 100).

Although the comment suggested a revision, it agreed in principle with the warning “Not to be applied over deep or puncture wounds, infections, or

lacerations. Consult a doctor.” A second comment requested, in the interest of brevity, clarity, and conservation of scarce label space, that the warning be shortened to read: “Do not apply over deep or puncture wounds or infections.”

The agency discussed the importance of each of the proposed warnings in comments 25 through 31 of the TFM (48 FR 6820 at 6828 to 6830) and stated that these warnings are necessary for petrolatum used as a skin protectant. In comment 31 of the TFM, however, the agency proposed not to require the “For external use only warning” for all products (including those containing petrolatum) formulated as lip balms. The agency is finalizing that proposal in this document.

In this final monograph, products containing the skin protectant ingredients mineral oil or sodium bicarbonate may omit the “For external use only” warning if they also provide labeling for oral use of the product. The agency believes that it could be confusing to consumers if products that contain petrolatum do not have the “For external use only” warning. Therefore, the agency is not exempting petrolatum (except in lip protectant products) from the “For external use only” warning in §§ 201.66(c)(5)(i) and 347.50(c)(1).

The agency considers the warning about not getting the product into the eye useful to help prevent possible improper use of skin protectant drug products which are often marketed in nonsterile, multiple use containers. The agency believes that the first comment misconstrued the purpose of the “if condition worsens” warning (§ 347.50(c)(3) of this final monograph). The warning is intended to direct consumers to seek medical attention for a condition if it gets worse or has not improved after 7 days of treatment and not to set 7 days as a maximum safe treatment period. The agency has

shortened this warning for products containing petrolatum (or white petrolatum) as a single ingredient to state: “See a doctor if condition lasts more than 7 days.”

With regard to the suggestion that the warning in § 347.50(c)(4) be revised, after the submission of this comment, the agency published a similar warning for OTC first aid antibiotic drug products (52 FR 47312 at 47324, December 11, 1987) and OTC first aid antiseptic drug products (56 FR 33644 at 33677, July 22, 1991). The agency is revising the warning in § 347.50(c)(4), accordingly, in the new format required by § 201.66.

(Comment 30) One comment considered the two general warnings in § 330.1(g) unnecessary for 100 percent petrolatum. The comment cited two references (Refs. 99 and 100) to support its contention that petrolatum is a uniquely safe OTC drug and presents no risk to the health of children from misuse, overuse, or abuse.

The agency finds the information in the cited references (as well as the information in § 172.880 regarding the regulation of petrolatum as an approved food additive) insufficient to support an exemption for 30 to 100 percent petrolatum from the two general warnings in § 330.1(g). References 99 and 100 list petrolatum concentrations at 0.02 to 5 percent, significantly lower than the concentration range included in the monograph. The agency revised the wording of these warnings in § 330.1(g) in the final rule for the new OTC drug product labeling format (64 FR 13254 at 13294).

(Comment 31). One comment stated that the agency’s proposed directions for sodium bicarbonate for use as a soak in a tub allow for a topical use concentration of about 0.3 percent, which is less than the dosage range for topical use of 1 to 100 percent (54 FR 40808 at 40818).

The agency has reviewed its calculations and agrees with the comment that the proposed directions for use as a soak in a tub allow for a topical concentration of less than 1 percent, depending on the amount of water in the tub and the size of the cup used. However, these directions are consistent with those suggested in the literature (Refs. 101 through 104). When these measurements are made by consumers, they may not be precise. Accordingly, in this final monograph, the agency recognizes that it is not possible or critical to make a precise determination of the use concentration for this ingredient. Thus, the agency has revised its recommendations.

(Comment 32) The agency has considered topical starch (formerly known as corn starch) in several rulemakings. In the advance notice of proposed rulemaking for OTC skin protectant drug products (43 FR 34628 at 34636), the TFM for OTC skin protectant drug products (48 FR 6820 at 6828), the TFM for OTC skin protectant poison ivy, poison oak, poison sumac, and insect bites drug products (54 FR 40808 at 40811 to 40812), the Miscellaneous External Panel's statement on OTC diaper rash drug products (47 FR 39436 at 39439, September 7, 1982), the TFM for OTC skin protectant diaper rash drug products (55 FR 25204 at 25232), and the TFM (53 FR 30756 at 30782) and final monograph (55 FR 31776 at 31780) for OTC anorectal drug products.

Based on the evaluations of the Topical Analgesic, Miscellaneous External, and Hemorrhoidal Panels, and the subsequent inclusion of topical starch as a protectant in the final monograph for OTC anorectal drug products and in the TFM for OTC diaper rash drug products, the agency is including topical starch at a concentration of 10 to 98 percent as an active ingredient under § 347.10(q) of this final monograph for OTC skin protectant drug products. The agency is including a minor skin irritation indication for the skin protectant

uses of topical starch in § 347.50(b)(6). Because topical starch should not be used on broken skin, other conditions (e.g., cuts, scrapes, chapped/cracked skin and lips) are not included in this final monograph. Warnings applicable to topical starch drug products in a powder dosage form are included in § 347.50(c)(6).

(Comment 33) Two comments from the same company requested that vitamins A and D be added to the list of Category I active ingredients in the skin protectant monograph. The comments stated that shark liver oil, which contains significant quantities of vitamins A and D, is an oleaginous substance that provides lubricity and emolliency. The comments mentioned that vitamins A and D, like cod and shark liver oils, have an emollient nature that provides a physical barrier to an irritant and aids in the temporary relief of minor skin irritations. The comments added that these oleaginous substances can lessen dermal injury caused by friction and lessen itching and dryness caused by water loss from the stratum corneum, thereby providing additional protection for exposed skin. The comments cited the Hemorrhoidal Panel's recommendations on the safety and topical use of vitamins A and D (45 FR 35576 at 35630 and 35634). Another comment stated that a number of the claims recommended by the Hemorrhoidal Panel in the advance notice of proposed rulemaking for OTC skin protectant drug products (43 FR 34628 at 34648) should be listed in the monograph for the ingredients vitamin A and vitamin D.

The Hemorrhoidal Panel did not review vitamin A or vitamin D (cholecalciferol) as single ingredients for use as protectants in OTC anorectal drug products but did consider these ingredients in its review of ingredients used for wound healing (45 FR 35576 at 35655 and 35656). The Hemorrhoidal

Panel concluded that the data submitted were insufficient to prove effectiveness of vitamins A and D as wound healing agents and classified these ingredients in Category III for this use (45 FR 35576 at 35655 and 35656). The agency did not include vitamins A or D in the anorectal final monograph because no data were submitted to support the effectiveness of these ingredients for protectant uses. However, the Hemorrhoidal Panel recommended that cod liver and shark liver oils be included in the Category I list of active ingredients for use as protectants in OTC anorectal drug products (45 FR 35576 at 35630 and 35634) and the agency concluded that these oils are monograph ingredients (55 FR 31776 at 31780). The agency pointed out in its proposed rulemaking for OTC diaper rash drug products (55 FR 25204 at 25225) that vitamins A and D have not been classified as skin protectants in any rulemaking in the OTC drug review, concluded that additional data are needed, and placed these ingredients in Category III.

Because no data were submitted to support the effectiveness of vitamins A and D for skin protectant uses, the agency concludes that these ingredients are nonmonograph when used individually or in combination other than as a component of cod liver oil listed in § 347.10(e) of this final monograph.

(Comment 34) In the TFM for OTC first aid antiseptic drug products (56 FR 33644 at 33650), the agency deferred data on a physical barrier cream product with protective claims to the rulemaking for OTC skin protectant drug products. The cream product contains a combination of ingredients: Cetyl alcohol, glyceryl stearate, isopropyl palmitate, stearyl alcohol, and beeswax, labeled as “skin wound protectant” ingredients. The product labeling states “helps protect minor cuts, burns, and skin irritations against contamination.” This claim is very similar to the claim included in § 347.50(b)(1) of this final

monograph. The submission included the results of animal and human safety studies on the finished product, including LD50 in mice and rats, acute dermal toxicity studies in rabbits, 48-hour and 72-hour primary irritation studies in humans using occlusive patch tests, and 21-day cumulative irritation studies. The submission also included reports of studies on the cream product's protective barrier effect and a clinical study to evaluate safety and effectiveness. The clinical study was described as a randomized, controlled, double-blind, parallel-group comparison of two products to determine the cream product's safety and effectiveness under actual use conditions. The control formulation was not provided.

The agency finds the submitted data insufficient to establish the skin protectant effect of any of the ingredients present in the cream product because the contribution, if any, of each of the individual active ingredients cannot be determined. The Panel recommended that there need be no limit to the number of skin protectant ingredients that may be combined in a product (43 FR 34628 at 34631). However, each ingredient must make a contribution to the claimed effect(s) in order to be deemed an active ingredient (§ 330.10(a)(4)(iv)). Further, the agency notes that the Miscellaneous External Panel classified the ingredients cetyl alcohol and stearyl alcohol as inactive in the advance notice of proposed rulemaking for OTC alcohol drug products (47 FR 22324 at 22326, May 21, 1982). In addition, the Dental Panel classified beeswax as inactive in the advance notice of proposed rulemaking for OTC drug products for the relief of oral discomfort (47 FR 22712 at 22715). No additional data on these three ingredients have been submitted to any rulemaking in the OTC drug review. The other two listed active ingredients, glyceryl stearate and isopropyl palmitate, have not been considered in any

rulemaking in the OTC drug review. Consequently, the agency concludes that the safety and effectiveness data are insufficient on beeswax, cetyl alcohol, glyceryl stearate, isopropyl palmitate, and stearyl alcohol. Therefore, these ingredients are being included in § 310.545(a)(18) as nonmonograph.

(Comment 35) Two comments contended that, as a class, skin protectant ingredients may be combined with more different types of therapeutic categories than any other class of ingredients. However, in the TFM, proposed § 347.20 does not list any ingredients other than skin protectant ingredients that may be combined. The comments stated that skin protectant ingredients have been found appropriate for use in combination with several other ingredient categories in other OTC drug product rulemakings. The comments requested that the agency include a provision in the final monograph allowing the combination of skin protectant ingredients with any therapeutic class of ingredients when such a combination has been found appropriate by any other OTC advisory review panel.

Proposed § 347.20 in the skin protectant TFM was published in the **Federal Register** on February 15, 1983, before the TFMs for many other categories of OTC drug products. Subsequently, based on panel recommendations in other OTC drug rulemakings and the TFMs for OTC external analgesic drug products (48 FR 5852 at 5868), OTC first aid antiseptic drug products (56 FR 33644 at 33677), and OTC sunscreen drug products (58 FR 28194 at 28296, May 12, 1993), this final monograph includes skin protectant active ingredients in combination with other ingredients from these therapeutic classes.

Therefore, the agency has further considered and expanded the ingredient combinations included in § 347.20 of this final monograph, including skin

protectant-sunscreen combinations in § 347.20(d). The agency is also amending the final monograph for OTC sunscreen drug products (64 FR 27666, May 21, 1999) to include sunscreen-skin protectant drug products. Further, the agency may be expanding the permitted combinations in § 347.20(b) and (c) as data submitted to the rulemakings for OTC external analgesic and first aid antiseptic drug products are evaluated and the final monographs for those OTC drug classes are issued.

III. Conclusion

Based on the available evidence, the agency is issuing a final monograph establishing conditions under which OTC skin protectant drug products are generally recognized as safe and effective and not misbranded. Any drug product labeled, represented, or promoted for use as an OTC skin protectant drug that contains any of the ingredients listed in § 310.545(a)(18)(i)(A) or (a)(18)(i)(B) or that is not in conformance with the monograph (part 347) may be considered a new drug within the meaning of section 201(p) of the act (21 U.S.C. 321(p)) and misbranded under section 502 of the act. Such a drug product cannot be marketed for skin protectant uses unless it is the subject of an approved application under section 505 of the act (21 U.S.C. 355) and part 314 of the regulations (21 CFR part 314). An appropriate citizen petition to amend the monograph may also be submitted in accord with 21 CFR 10.30 and 330.10(a)(12)(i). Any OTC skin protectant drug product initially introduced or initially delivered for introduction into interstate commerce after the compliance dates of the final rule for § 310.545(a)(18)(i)(A) or this final rule that is not in compliance with the regulations is subject to regulatory action.

Our decision to revise the warnings set forth in this final rule is based on comments made in response to the proposed rule. Mandating warnings in an OTC drug monograph does not require a finding that any or all of the OTC drug products covered by the monograph actually caused an adverse event, and FDA does not so find. Nor does FDA's requirement of warnings repudiate the prior OTC drug monographs and monograph rulemakings under which the affected drug products have been lawfully marketed. Rather, as a consumer protection agency, FDA has determined that warnings are necessary to ensure that these OTC drug products continue to be safe and effective for their labeled indications under ordinary conditions of use as those terms are defined in the act. This judgment balances the benefits of these drug products against their potential risks (see 21 CFR 330.10(a)).

FDA's decision to act in this instance need not meet the standard of proof required to prevail in a private tort action (*Glastetter v. Novartis Pharmaceuticals, Corp.*, 252 F. 3d 986, 991 (8th Cir. 2001)). To mandate warnings, or take similar regulatory action, FDA need not show, nor do we allege, actual causation. For an expanded discussion of case law supporting FDA's authority to require such warnings, see the final rule entitled "Labeling of Diphenhydramine-Containing Drug Products for Over-the-Counter Human Use" (67 FR 72555, December 6, 2002).

IV. Labeling Guidance

In the **Federal Register** of March 17, 1999 (64 FR 13254), FDA established a standardized format and standardized content for the labeling of OTC drug products. Table 1 of this document shows how the warnings proposed in the TFM have been revised in this final rule based on comments received and

using the new format in § 201.66. Using the format in § 201.66(c)(4), the warnings in §§ 347.50(c) and 347.52(c) appear as follows:

TABLE 1.—REVISION OF PROPOSED MONOGRAPH WARNINGS TO NEW FORMAT

Skin Protectant Tentative Final Monograph	Skin Protectant Final Monograph
Not to be applied over deep or puncture wounds, infections, or lacerations. Consult a doctor. Do not use on broken skin.	Do not use on <ul style="list-style-type: none"> • deep puncture wounds • serious burns <ul style="list-style-type: none"> • animal bites • broken skin¹
Avoid contact with the eyes. Keep powder away from child's face to avoid inhalation, which can cause breathing problems. Take special care to avoid slipping when getting into and out of the tub.	When using this product <ul style="list-style-type: none"> • do not get into eyes • keep away from face and mouth to avoid breathing it • in some skin conditions, soaking too long may overdry • to avoid slipping, use mat in tub or shower
If condition worsens or does not improve within 7 days, consult a doctor.	Stop use and ask doctor if <ul style="list-style-type: none"> • condition worsens • symptoms last more than 7 days or clear up and occur again within a few days
For external use only.	For external use only ²

¹ Only required for powder products containing kaolin or topical starch. See § 347.50(c)(6).

² In bold type on the line immediately following the line for the Warnings heading. See § 201.66(c)(5)(i) and (d)(6).

Section 201.66(d)(10) (21 CFR 201.66(d)(10)), which sets forth format and content requirements for OTC drug product labeling, establishes a modified labeling format for small packages that need more than 60 percent of their total surface area available to bear labeling to meet the format requirements of § 201.66(d)(1) through (d)(9). The agency stated in the final rule that established these labeling requirements that it would consider additional approaches for accommodating certain products in their respective monographs, taking into consideration the risks and benefits of the drug, the intended use, and the need to communicate limitations or restrictions about the use of the product to the target population (64 FR 13254 at 13270).

In the final monograph for OTC sunscreen drug products (64 FR 27666 at 27678), the agency discussed modified warnings for lip balm products and stated that it expects to adopt the same modifications when it issues the final monograph for OTC skin protectant drug products. Accordingly, the agency is establishing additional labeling exemptions for lip balm/lip protectant products that meet the criteria established in § 201.66(d)(10). The specifications for products formulated and labeled as a lip protectant or lip

balm that meet the criteria established in § 201.66(d)(10) are in § 347.50(e) of the skin protectant final monograph. In making this determination for lip protectant/lip balm products, the agency considered a number of factors that were discussed in the final rule that established the new OTC drug product labeling format in § 201.66 (64 FR 13254 at 13270). These factors include the risks and benefits of the drug, the intended use, and the need to communicate limitations or restrictions about the use of the product to the target population. Lip protectant/lip balm products are typically packaged in small amounts, applied to limited areas of the body, have a high therapeutic index, carry extremely low risk in actual consumer use situations, provide a favorable public health benefit, require no specified dosage limitation, and require few specific warnings and no general warnings (e.g., pregnancy or overdose warnings). For these reasons, the agency has concluded that minimal information is needed for the safe and effective use of such products.

The agency is also including in this final rule some modified labeling requirements in § 347.50(f) of the final monograph for products containing only cocoa butter, petrolatum, or white petrolatum singly or in combination with each other when marketed other than as a lip protectant or lip balm. In making this decision for cocoa butter, the agency considered the factors discussed in the previous paragraphs and the Panel's recommendations on cocoa butter. The Panel stated in its safety evaluation of cocoa butter (43 FR 34628 at 34635) that "No reports regarding the safety of cocoa butter have been specifically identified. However, the Panel recognizes that its safety has been established by its wide and continuous use in pharmaceutical products and cosmetics. Clinical and marketing experience has confirmed that cocoa butter is safe in the dosage range used as a skin protectant." Thus, these products have an

extremely low risk in actual consumer use situations. In addition, the agency has considered the OTC uses for this ingredient as providing temporary protection of minor cuts, scrapes, burns, and chapped or cracked skin and lips. Application to these areas for these uses will likely be infrequent and to limited areas of the body. In making this decision for petrolatum and white petrolatum, the agency considered the factors discussed in the previous paragraphs, the Panel's recommendations, and the evidence and data described in section II., comment 29 of this document. The Panel stated in its safety evaluation of petrolatum preparations (43 FR 34628 at 34639) that "Petrolatum is not absorbed through intact or injured skin and is neither sensitizing nor irritating. Large amounts are essentially nontoxic when ingested in liquid laxative preparations. Clinical and marketing experience has confirmed that petrolatum is safe in the OTC dosage range used as a skin protectant." As noted for cocoa butter, the agency has considered the OTC uses for these ingredients and believes that application to these areas for these uses will likely be infrequent and to limited areas of the body. The agency concludes that petrolatum and white petrolatum have an extremely low risk in actual consumer use situations. Moreover, both products provide a favorable public health benefit, require no specified dosage limitation, and require few specific warnings and no general warnings (e.g., pregnancy or overdose warnings).

V. Stay of § 347.20(d) and Part 352

The agency is lifting the stay for the sunscreen monograph in part 352 for the sole purpose of amending the codified language as set forth in the skin protectant final monograph. Once the codified language is amended, part 352 will remain stayed indefinitely. The agency is also staying § 347.20(d) because

it involves combination products that contain sunscreen active ingredients. To the extent that 5 U.S.C. 553 applies to this action, it is exempt from notice and comment because it constitutes a rule of procedure under 5 U.S.C. 553(b)(3)(A). Alternatively, the agency's implementation of this action without opportunity for public comment comes within the good cause exceptions in 5 U.S.C. 553(b)(3)(B) in that obtaining public comment is impracticable, unnecessary, and contrary to the public interest. The agency complied with the notice and comment procedures in 5 U.S.C. 553 when it issued the skin protectant final monograph set forth in this notice. The agency is lifting the stay for part 352 in order to revise part 352 to be consistent with that monograph. As the agency stated in the **Federal Register** of December 31, 2001 (66 FR 67485), FDA intends to publish a proposal to amend part 352 in order to develop a comprehensive sunscreen monograph that addresses formulation, labeling, and testing requirements for both ultraviolet B (UVB) and ultraviolet A (UVA) radiation protection. That amendment will propose a new effective date for part 352 and for § 347.20(d). Thus, there will be an opportunity for public comment on the new effective date within the proposed amendment to part 352. In accordance with 21 CFR 10.40(e)(1), FDA is providing an opportunity for comment on whether this partial stay should be modified or revoked.

VI. Analysis of Impacts

An analysis of the costs and benefits of this regulation, conducted under Executive Order 12291, was discussed in the TFM for OTC skin protectant drug products (48 FR 6820 at 6831). The agency certified that under the Regulatory Flexibility Act the proposed rule would not have a significant economic impact

on a substantial number of small entities. No comments were received on the economic impact of this rulemaking.

FDA has examined the impacts of the final rule under Executive Order 12866, the Regulatory Flexibility Act (5 U.S.C. 601–612), and the Unfunded Mandates Reform Act of 1995 (2 U.S.C. 1501 *et seq.*). Executive Order 12866 directs agencies to assess all costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages; distributive impacts; and equity). Under the Regulatory Flexibility Act, if a rule may have a significant economic impact on a substantial number of small entities, an agency must analyze regulatory options that would minimize any significant impact of the rule on small entities. Section 202(a) of the Unfunded Mandates Reform Act of 1995 requires that agencies prepare a written statement and economic analysis before proposing any rule that may result in an expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of \$100 million in any one year (adjusted annually for inflation). The proposed rules that have led to the development of this final rule were published on February 15, 1983, and October 3, 1989, before the Unfunded Mandates Reform Act of 1995 was enacted. The agency explains in this final rule that the final rule will not result in an expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of \$100 million in any one year.

The agency concludes that this final rule is consistent with the principles set out in Executive Order 12866 and in these two statutes. The final rule is not a significant regulatory action as defined by the Executive order and so is not subject to review under the Executive order. The Unfunded Mandates

Reform Act does not require FDA to prepare a statement of costs and benefits for this final rule, because the final rule is not expected to result in any 1-year expenditure that would exceed \$100 million adjusted for inflation. The current inflation adjusted statutory threshold is about \$110 million.

The purpose of this final rule is to establish allowable monograph ingredients and labeling under which OTC skin protectant drug products are generally recognized as safe and effective. Of the 29 active ingredients considered in this final rule, 19 are being included in the final monograph while 10 are not. Of the 10 not included, 1 is deferred to the final rule on OTC skin protectant diaper rash drug products and 1 may be included pending development of a USP/NF monograph for the ingredient.

Products containing the remaining eight active ingredients will need to be reformulated to delete and replace the ingredient(s) with another (monograph) skin protectant active ingredient or an inactive vehicle. As discussed in section II, comment 34 of this document, at least three and maybe five of these eight ingredients also could be used as inactive (vehicle) ingredients in topical drug products. Therefore, some of these manufacturers may be able to relabel their products without reformulations to comply with this rule.

The agency's Drug Listing System identifies approximately 4,000 drug products containing these 8 ingredients; however, only a limited number of these products list these ingredients as active for a skin protectant drug product (table 2) in the next paragraph of this document.

TABLE 2.—NUMBER OF MARKETERS AND PRODUCTS LISTING INGREDIENTS AS ACTIVE

Ingredient	No. of Marketers	No. of Products
Beeswax	2	2
Boric acid	21	22
Cetyl alcohol	3	9

The cost to reformulate a product will vary greatly depending on the nature of the change in formulation, the product, the process, and the size of the firm. Some of the 33 manufacturers of the 50 products containing nonmonograph active ingredients may not have to reformulate. For those products that need reformulation, the cost can be significant. Because of the large number of monograph active ingredients available for reformulation, no manufacturer should need to change its dosage form; however, it will have to redo the validation (product, process, new supplier), conduct stability tests, and change master production records. The agency estimates the cost of reformulation to range from \$100,000 to \$500,000. Therefore, if all 50 products are reformulated, the midpoint of the cost estimate implies total costs of \$15 million. However, the agency believes the total costs will be much smaller because not all manufacturers will have to reformulate and some may choose to discontinue a product line if sales are too low to justify the added cost and/or they also produce substitute products that do not require reformulation.

Because these products must be manufactured in compliance with the pharmaceutical current good manufacturing practices (21 CFR parts 210 and 211), all firms would have the necessary skills and personnel to perform these tasks either in-house or by contractual arrangement. No additional professional skills are needed.

This final rule establishes the monograph for OTC skin protectant drug products and will require relabeling of all products covered by the monograph. The agency's Drug Listing System identifies approximately 1,300 OTC skin protectant drug products containing the 29 ingredients covered by this final rule. It is likely that there are a number of additional products that are not currently included in the agency's system. Also, as indicated previously, a

number of the skin protectant ingredients can be and often are used as inactive ingredients in many of the OTC drug products included in the Drug Listing System. While it is difficult to determine an exact number, the agency estimates that 2,000 to 2,500 OTC stockkeeping units (SKUs) (individual products, packages, and sizes) will need to be relabeled based on this final rule. Based on information in the Drug Listing System, the agency estimates there are at least 200 manufacturers and 700 marketers of these products. Marketers, however, generally do not incur these costs because manufacturers of OTC drug products are usually responsible for product labeling, testing, and formulation.

Estimates of relabeling costs for the type of changes required by this rule vary greatly and range from \$500 to \$15,000 per SKU depending on whether the products are nationally branded or private label. The agency assumes the same weighted average cost to relabel (i.e., \$3,600 per SKU) that it estimated for the final rule requiring uniform label formats of OTC drug products (64 FR 13254 at 13279 to 13281). Assuming 2,000 to 2,500 affected OTC SKUs in the marketplace, total one-time costs of relabeling would be \$7.2 to \$9.0 million. Because frequent labeling redesigns are a recognized cost of doing business in the OTC drug industry, these costs may be less. Manufacturers that make voluntary market-driven changes to their labeling during the implementation period can implement the regulatory requirements for a nominal cost. The final rule would not require any new reporting or recordkeeping activities.

This final rule may have an economic impact on some small entities. The agency's Drug Listing System indicates that about 700 marketers will need to relabel, and that this relabeling will be prepared by about 200 manufacturers,

most of which are private label or contract manufacturers. Based on the Small Business Administration's determination that a small firm in this industry has fewer than 750 employees, roughly 70 percent of the firms are considered small. The economic impact on any particular firm is very difficult to measure, because it will vary with the type and number of products affected, the number of SKUs per product, and the ability to coordinate these label changes with those required for other purposes. For example, assuming average industry costs, a small company that had 5 products with 3 SKUs each, for a total of 15 SKUs, would experience a one-time cost of \$54,000 ($15 \times \$3,600$). A small private label manufacturer with the same product line and 10 customers per SKU, for a total of 150 SKU's, would experience a one-time cost of \$540,000 ($150 \times \$3,600$). If one or more products needed to be reformulated, the costs would increase by \$100,000 to \$500,000 per reformulation. Some of these relabeling costs may be mitigated to the extent that manufacturers can coordinate this relabeling with relabeling requirements for the standardized format and content labeling requirements of OTC drug products (§ 201.66) and the sunscreen rule. Products with annual sales less than \$25,000 have 1 additional year. Therefore, many of the labeling revisions may be done in the normal course of business. These steps should help to minimize the impact on small entities by providing enough time for implementation to enable entities to use up existing labeling stock. The agency believes that these actions provide substantial flexibility and reductions in cost for small entities.

The agency considered but rejected several labeling alternatives: (1) A shorter or longer implementation period, and (2) an exemption from coverage for small entities. While the agency believes that consumers would benefit from having this new labeling in place as soon as possible, a longer time period

would unnecessarily delay the benefit of new labeling and revised formulations, where applicable, to consumers. The agency rejected an exemption for small entities because the new labeling and revised formulations, where applicable, are also needed by consumers who purchase products marketed by those entities. However, a longer (24-month) compliance date is being provided for products with annual sales less than \$25,000.

This analysis shows that the agency has undertaken important steps to reduce the burden to small entities. Thus, this economic analysis, together with other relevant sections of this document, serves as the agency's final regulatory flexibility analysis, as required under the Regulatory Flexibility Act.

VII. Paperwork Reduction Act of 1995

FDA concludes that the labeling requirements in this document are not subject to review by the Office of Management and Budget because they do not constitute a "collection of information" under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501 *et seq.*). Rather, the labeling statements are a "public disclosure of information originally supplied by the Federal Government to the recipient for the purpose of disclosure to the public" (5 CFR 1320.3(c)(2)).

VIII. Federalism

FDA has analyzed this final rule in accordance with the principles set forth in Executive Order 13132. FDA has determined that the rule does not contain policies that have substantial direct effects on the States, on the relationship between National Government and the States, or on the distribution of power and responsibilities among the various levels of government. Accordingly, the agency has concluded that the rule does not

contain policies that have federalism implications as defined in the Executive order and, consequently, a federalism summary impact statement is not required.

IX. Environmental Impact

The agency has determined under 21 CFR 25.31(a) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

X. Request for Comments

This final rule includes reduced labeling requirements for products formulated and labeled as a lip protectant that meet the criteria established in § 201.66(d)(10) (see § 347.60(e)); for products containing only cocoa butter, petrolatum, or white petrolatum identified in § 347.10(d), (m), and (r), used singly or in combination with each other, and marketed other than as a lip protectant (see § 347.60(f)); for sunscreen drug products labeled for use only on specific small areas of the face (e.g., lips, nose, ears, and/or around eyes) and that meet the criteria established in § 201.66(d)(10) (see § 352.52(f)); and for combinations of skin protectant and sunscreen active ingredients (see § 352.60(b)(2), (c), and (d)). Some of this reduced labeling results from the modified labeling format for OTC drug products in § 201.66(d)(10), which did not exist when the TFM and amended TFM were published. Some of this reduced labeling is in response to comments specifically addressing petrolatum and white petrolatum, which the agency has extended to cocoa butter. The agency is providing 90 days for comment on the specific labeling requirements discussed in this section. Comments should be identified with the docket

number found in brackets in the heading of this document. Three copies of all mailed comments are to be submitted. Individuals submitting written comments or anyone submitting electronic comments may submit one copy. Received comments may be seen in the Dockets Management Branch (see **ADDRESSES**) between 9 a.m. and 4 p.m., Monday through Friday. If the comments justify a change in labeling, the agency will propose to amend the final monographs accordingly at a later date. Because the amendment process can take a significant period of time, manufacturers of the products covered by this final rule should implement the labeling stated therein at this time, unless the compliance date has been stayed.

XI. References

The following references are on display in the Dockets Management Branch (see **ADDRESSES**) and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday.

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21. OTC Vol. 160034.
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23. Comment No. C00062, Docket No. 78N–0021, Dockets Management Branch.
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99. Oser, B. L. et al., "Toxicologic Studies of Petrolatum in Mice and Rats," *Toxicology and Applied Pharmacology* 7:382-401, 1965.

100. *Foods Chemicals Codex*, 3d ed., National Academy Press, Washington, DC, p. 221, 1981.

101. Lyght, E. E., ed., *The Merck Manual*, 9th ed., Merck & Co., Rahway, NJ, p. 1756, 1956.

102. Sollmann, T., *A Manual of Pharmacology*, 7th ed., W. B. Saunders Co., Philadelphia, PA, p. 122, 1948.

103. Schalek, A., *Fundamentals of Dermatology*, 2d ed., Lea & Febiger, Philadelphia, PA, p. 34, 1931.

104. Tobias, N., *Essentials of Dermatology*, 4th ed., J. B. Lippincott Co., Philadelphia, PA, p. 552, 1952.

List of Subjects

21 CFR Part 310

Administrative practice and procedure, Drugs, Labeling, Medical devices, Reporting and recordkeeping requirements.

21 CFR Parts 347 and 352

Labeling, Over-the-counter drugs.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, 21 CFR parts 310, 347, and 352 are amended as follows:

PART 310—NEW DRUGS

1. The authority citation for 21 CFR part 310 continues to read as follows:

Authority: 21 U.S.C. 321, 331, 351, 352, 353, 355, 360b-360f, 360j, 361(a), 371, 374, 375, 379e; 42 U.S.C. 216, 241, 242(a), 262, 263b-263n.

2. Section 310.545 is amended by revising paragraphs (a)(18)(i), (a)(18)(v), (a)(18)(vi), and (d)(1), and by adding paragraph (d)(32) to read as follows:

§ 310.545 Drug products containing certain active ingredients offered over-the-counter (OTC) for certain uses.

(a) * * *

(18) * * *

(i)(A) *Ingredients—Approved as of May 7, 1991.*

Allantoin (wound healing claims only)

Sulfur

Tannic acid

Zinc acetate (wound healing claims only)

(B) *Ingredients—Approved as of [insert date 12 months after date of publication in the **Federal Register**]; [insert date 24 months after date of publication in the **Federal Register**], for products with annual sales less than \$25,000.*

Beeswax

Bismuth subnitrate

Boric acid

Cetyl alcohol

Glyceryl stearate

Isopropyl palmitate

Live yeast cell derivative

Shark liver oil

Stearyl alcohol

* * * * *

(v) *Insect bite and sting drug products.*

(A) *Ingredients—Approved as of May 7, 1991.*

Alcohol

Alcohol, ethoxylated alkyl

Ammonia solution, strong

Ammonium hydroxide

Benzalkonium chloride

Camphor

Ergot fluid extract

Ferric chloride

Menthol

Peppermint oil

Phenol

Pyrilamine maleate

Sodium borate

Trolamine

Turpentine oil

Zirconium oxide

*(B) Ingredients—Approved as of [insert date 12 months after date of publication in the **Federal Register**]; [insert date 24 months after date of publication in the **Federal Register**], for products with annual sales less than \$25,000.*

Beeswax

Bismuth subnitrate

Boric acid

Cetyl alcohol

Glyceryl stearate

Isopropyl palmitate

Live yeast cell derivative

Shark liver oil

Stearyl alcohol

* * * * *

(vi) *Poison ivy, poison oak, and poison sumac drug products.*

(A) *Ingredients—Approved as of May 7, 1991.*

Alcohol

Anion and cation exchange resins buffered

Benzethonium chloride

Benzocaine

Benzyl alcohol

Bismuth subnitrate

Bithionol

Boric acid

Camphor

Cetalkonium chloride

Chloral hydrate

Chlorpheniramine maleate

Creosote

Diperodon hydrochloride

Diphenhydramine hydrochloride

Eucalyptus oil

Ferric chloride

Glycerin

Hectorite

Hydrogen peroxide

Impatiens biflora tincture

Iron oxide

Isopropyl alcohol

Lanolin

Lead acetate

Lidocaine

Menthol

Merbromin

Mercuric chloride

Panthenol

Parethoxycaine hydrochloride

Phenol

Phenyltoloxamine dihydrogen citrate

Povidone-vinylacetate copolymers

Salicylic acid

Simethicone

Tannic acid

Topical starch

Trolamine

Turpentine oil

Zirconium oxide

Zyloxin

(B) *Ingredients—Approved as of [insert date 12 months after date of publication in the **Federal Register**]; [insert date 24 months after date of*

*publication in the **Federal Register**], for products with annual sales less than \$25,000.*

Beeswax

Bismuth subnitrate

Boric acid

Cetyl alcohol

Glyceryl stearate

Isopropyl palmitate

Live yeast cell derivative

Shark liver oil

Stearyl alcohol

* * * * *

(d) * * *

(1) May 7, 1991, for products subject to paragraphs (a)(1) through (a)(2)(i), (a)(3)(i), (a)(4), (a)(6)(i)(A), (a)(6)(ii)(A), (a)(7) (except as covered by paragraph (d)(3) of this section), (a)(8)(i), (a)(10)(i) through (a)(10)(iii), (a)(12)(i) through (a)(12)(iv)(A), (a)(14) through (a)(15)(i), (a)(16) through (a)(18)(i)(A), (a)(18)(ii) (except as covered by paragraph (d)(22) of this section), (a)(18)(iii), (a)(18)(iv), (a)(18)(v)(A), and (a)(18)(vi)(A) of this section.

* * * * *

(32) [*insert date 12 months after date of publication in the **Federal Register***], for products subject to paragraphs (a)(18)(i)(B), (a)(18)(v)(B), and (a)(18)(vi)(B) of this section. [*insert date 24 months after date of publication in the **Federal Register***], for products with annual sales less than \$25,000.

PART 347—SKIN PROTECTANT DRUG PRODUCTS FOR OVER-THE-COUNTER HUMAN USE

3. The authority citation for 21 CFR part 347 continues to read as follows:

Authority: 21 U.S.C. 321, 351, 352, 353, 355, 360, 371.

4. Part 347 is amended by revising the heading for subpart A to read as follows:

Subpart A—General Provisions

* * * * *

5. Section 347.3 is revised to read as follows:

§ 347.3 Definitions.

As used in this part:

Astringent drug product. A drug product applied to the skin or mucous membranes for a local and limited protein coagulant effect.

Lip protectant drug product. A drug product that temporarily prevents dryness and helps relieve chapping of the exposed surfaces of the lips; traditionally called “lip balm.”

Poison ivy, oak, sumac dermatitis. An allergic contact dermatitis due to exposure to plants of the genus *Rhus* (poison ivy, poison oak, poison sumac), which contain urushiol, a potent skin-sensitizer.

Skin protectant drug product. A drug product that temporarily protects injured or exposed skin or mucous membrane surfaces from harmful or annoying stimuli, and may help provide relief to such surfaces.

6. Section 347.10 is redesignated as § 347.12 and revised, and subpart B, consisting of a new § 347.10, newly redesignated § 347.12, and new § 347.20, is added to read as follows:

Subpart B—Active Ingredients

Sec.

347.10 Skin protectant active ingredients.

347.12 Astringent active ingredients.

347.20 Permitted combinations of active ingredients.

Subpart B—Active Ingredients**§ 347.10 Skin protectant active ingredients.**

The active ingredients of the product consist of any of the following, within the concentration specified for each ingredient:

(a) Allantoin, 0.5 to 2 percent.

(b) Aluminum hydroxide gel, 0.15 to 5 percent.

(c) Calamine, 1 to 25 percent.

(d) Cocoa butter, 50 to 100 percent.

(e) Cod liver oil, 5 to 13.56 percent, in accordance with § 347.20(a)(1) or (a)(2), provided the product is labeled so that the quantity used in a 24-hour period does not exceed 10,000 U.S.P. Units vitamin A and 400 U.S.P. Units cholecalciferol.

(f) Colloidal oatmeal, 0.007 percent minimum; 0.003 percent minimum in combination with mineral oil in accordance with § 347.20(a)(4).

(g) Dimethicone, 1 to 30 percent.

(h) Glycerin, 20 to 45 percent.

(i) Hard fat, 50 to 100 percent.

(j) Kaolin, 4 to 20 percent.

(k) Lanolin, 12.5 to 50 percent.

(l) Mineral oil, 50 to 100 percent; 30 to 35 percent in combination with colloidal oatmeal in accordance with § 347.20(a)(4).

(m) Petrolatum, 30 to 100 percent.

- (n) [Reserved]
- (o) Sodium bicarbonate.
- (p) [Reserved]
- (q) Topical starch, 10 to 98 percent.
- (r) White petrolatum, 30 to 100 percent.
- (s) Zinc acetate, 0.1 to 2 percent.
- (t) Zinc carbonate, 0.2 to 2 percent.
- (u) Zinc oxide, 1 to 25 percent.

§ 347.12 Astringent active ingredients.

The active ingredient of the product consists of any one of the following within the specified concentration established for each ingredient:

(a) Aluminum acetate, 0.13 to 0.5 percent (depending on the formulation and concentration of the marketed product, the manufacturer must provide adequate directions so that the resulting solution to be used by the consumer contains 0.13 to 0.5 percent aluminum acetate).

(b) Aluminum sulfate, 46 to 63 percent (the concentration is based on the anhydrous equivalent).

(c) Witch hazel.

§ 347.20 Permitted combinations of active ingredients.

(a) *Combinations of skin protectant active ingredients.* (1) Any two or more of the ingredients identified in § 347.10(a), (d), (e), (i), (k), (l), (m), and (r) may be combined provided the combination is labeled according to § 347.50(b)(1) and provided each ingredient in the combination is within the concentration specified in § 347.10.

(2) Any two or more of the ingredients identified in § 347.10(a), (d), (e), (g), (h), (i), (k), (l), (m), and (r) may be combined provided the combination

is labeled according to § 347.50(b)(2) and provided each ingredient in the combination is within the concentration specified in § 347.10.

(3) Any two or more of the ingredients identified in § 347.10(b), (c), (j), (s), (t), and (u) may be combined provided the combination is labeled according to § 347.50(b)(3) and provided each ingredient in the combination is within the concentration specified in § 347.10.

(4) The ingredients identified in § 347.10(f) and (l) may be combined provided the combination is labeled according to § 347.50(b)(7) and provided each ingredient in the combination is within the concentration specified in § 347.10.

(b) *Combinations of skin protectant and external analgesic active ingredients.* Any one (two when required to be in combination) or more of the active ingredients identified in § 347.10(a), (d), (e), (i), (k), (l), (m), and (r) may be combined with any of the following generally recognized as safe and effective external analgesic active ingredients: Single amine and “caine”-type local anesthetics, alcohols and ketones, antihistamines, or any permitted combination of these ingredients, but not with hydrocortisone, provided the product is labeled according to § 347.60(b)(l).

(c) *Combinations of skin protectant and first aid antiseptic active ingredients.* Any one (two when required to be in combination) or more of the active ingredients identified in § 347.10(a), (d), (e), (i), (k), (l), (m), and (r) may be combined with any generally recognized as safe and effective single first aid antiseptic active ingredient, or any permitted combination of these ingredients, provided the product is labeled according to § 347.60(b)(2).

(d) *Combinations of skin protectant and sunscreen active ingredients.* Any one (two when required to be in combination) or more of the skin protectant

active ingredients identified in § 347.10(a), (d), (e), (g), (h), (i), (k), (l), (m), and (r) may be combined with any generally recognized as safe and effective single sunscreen active ingredient, or any permitted combination of these ingredients, provided the product meets the conditions in § 352.20(b) of this chapter and is labeled according to §§ 347.60(b)(3) and 352.60(b) of this chapter.

7. Section 347.20(d) is stayed until further notice.

8. Section 347.50 is redesignated as § 347.52 and revised, and subpart C, consisting of a new § 347.50, newly redesignated § 347.52, and new § 347.60, is added to read as follows:

Subpart C—Labeling

Sec.

347.50 Labeling of skin protectant drug products.

347.52 Labeling of astringent drug products.

347.60 Labeling of permitted combinations of active ingredients.

Subpart C—Labeling

§ 347.50 Labeling of skin protectant drug products.

A skin protectant drug product may have more than one labeled use and labeling appropriate to different uses may be combined to eliminate duplicative words or phrases as long as the labeling is clear and understandable. When the labeling of the product contains more than one labeled use, the appropriate statement(s) of identity, indications, warnings, and directions must be stated in the labeling.

(a) *Statement of identity.* The labeling of the product contains the established name of the drug, if any, and identifies the product with one or more of the following:

(1) *For any product.* “Skin protectant” (optional, may add dosage form, e.g., “cream,” “gel,” “lotion,” or “ointment”).

(2) *For products containing any ingredient in § 347.10(b), (c), (j), (s), (t), and (u).* “Poison ivy, oak, sumac drying” (optional, may add dosage form, e.g., “cream,” “gel,” “lotion,” or “ointment”).

(3) *For products containing any ingredient in § 347.10(b), (c), (f), (j), (o), (s), (t), and (u).* “Poison ivy, oak, sumac protectant.”

(b) *Indications.* The labeling of the product states, under the heading “Uses,” one or more of the phrases listed in this paragraph (b), as appropriate. Other truthful and nonmisleading statements, describing only the uses that have been established and listed in this paragraph (b), may also be used, as provided in § 330.1(c)(2) of this chapter, subject to the provisions of section 502 of the Federal Food, Drug, and Cosmetic Act (the act) relating to misbranding and the prohibition in section 301(d) of the act against the introduction or delivery for introduction into interstate commerce of unapproved new drugs in violation of section 505(a) of the act.

(1) *For products containing any ingredient in § 347.10(a), (d), (e), (i), (k), (l), (m), and (r).* The labeling states “temporarily protects minor: [bullet]¹ cuts [bullet] scrapes [bullet] burns”.

(2) *For products containing any ingredient in § 347.10(a), (d), (e), (g), (h), (i), (k), (l), (m), and (r)—(i).* The labeling states “temporarily protects” (which may be followed by: “and helps relieve”) “chapped or cracked skin” (which may be followed by: “and lips”). This statement may be followed by the optional statement: “helps protect from the drying effects of wind and cold weather”. [If both statements are used, each is preceded by a bullet.]

¹ See § 201.66(b)(4) of this chapter for definition of bullet symbol.

(ii) *For products formulated as a lip protectant.* The labeling states “temporarily protects” (which may be followed by: “and helps relieve”) “chapped or cracked lips”. This statement may be followed by the optional statement: “helps protect lips from the drying effects of wind and cold weather”. [If both statements are used, each is preceded by a bullet.]

(3) *For products containing any ingredient in § 347.10(b), (c), (j), (s), (t), and (u).* The labeling states “dries the oozing and weeping of poison: [bullet] ivy [bullet] oak [bullet] sumac”.

(4) *For products containing colloidal oatmeal identified in § 347.10(f).* The labeling states “temporarily protects and helps relieve minor skin irritation and itching due to: [select one or more of the following: ‘[bullet] rashes’ ‘[bullet] eczema’ ‘[bullet] poison ivy, oak, or sumac’ ‘[bullet] insect bites’].”

(5) *For products containing sodium bicarbonate identified in § 347.10(o).* The labeling states “temporarily protects and helps relieve minor skin irritation and itching due to: [bullet] poison ivy, oak, or sumac [bullet] insect bites”.

(6) *For products containing topical starch identified in § 347.10(q).* The labeling states “temporarily protects and helps relieve minor skin irritation”.

(7) *For products containing the combination of ingredients in § 347.20(a)(4).* The labeling states “temporarily protects and helps relieve minor skin irritation and itching due to: [select one or more of the following: ‘rashes’ or ‘eczema’].” [If both conditions are used, each is preceded by a bullet.]

(c) *Warnings.* The labeling of the product contains the following warnings under the heading “Warnings”:

(1) “For external use only” in accord with § 201.66(c)(5)(i) of this chapter. For products containing only mineral oil in § 347.10(l) or sodium bicarbonate

in § 347.10(o), this warning may be omitted if labeling for oral use of the product is also provided.

(2) “When using this product [bullet] do not get into eyes”.

(3) “Stop use and ask a doctor if [bullet] condition worsens [bullet] symptoms last more than 7 days or clear up and occur again within a few days”.

(4) For products labeled according to § 347.50(b)(1) or (b)(2): “Do not use on [bullet] deep or puncture wounds [bullet] animal bites [bullet] serious burns”.

(5) For products containing colloidal oatmeal identified in § 347.10(f) when labeled for use as a soak in a tub. “When using this product [bullet] to avoid slipping, use mat in tub or shower”.

(6) For powder products containing kaolin identified in § 347.10(j) or topical starch identified in § 347.10(q)—(i) “Do not use on [bullet] broken skin”.

(ii) “When using this product [bullet] keep away from face and mouth to avoid breathing it”.

(7) For products containing colloidal oatmeal identified in § 347.10(f) or sodium bicarbonate identified in § 347.10(o) when labeled for use as a soak, compress, or wet dressing. “When using this product [bullet] in some skin conditions, soaking too long may overdry”.

(d) *Directions*. The labeling of the product contains the following statements, as appropriate, under the heading “Directions”:

(1) *For products labeled according to § 347.50(b)(1), (b)(2), (b)(3), (b)(5), or (b)(6).* The labeling states “apply as needed”.

(2) *For products containing colloidal oatmeal identified in § 347.10(f)—*
(i) *For products requiring dispersal in water.* The labeling states “[bullet] turn

warm water faucet on to full force [bullet] slowly sprinkle” (manufacturer to insert quantity to be used) “of colloidal oatmeal directly under the faucet into the tub or container [bullet] stir any colloidal oatmeal settled on the bottom”.

(A) *For products used as a soak in a bath.* The manufacturer must provide adequate directions to obtain a solution containing a minimum of 0.007 percent colloidal oatmeal or 0.003 percent colloidal oatmeal in the oilated form for a tub bath, sitz bath, or infant bath, or a minimum of 0.25 percent colloidal oatmeal for a foot bath. “For use as a soak in a bath: [bullet] soak affected area for 15 to 30 minutes as needed, or as directed by a doctor [bullet] pat dry (do not rub) to keep a thin layer on the skin”.

(B) *For products used as a compress or wet dressing.* The manufacturer must provide adequate directions to obtain a solution containing a minimum of 0.25 percent colloidal oatmeal. “For use as a compress or wet dressing: [bullet] soak a clean, soft cloth in the mixture [bullet] apply cloth loosely to affected area for 15 to 30 minutes [bullet] repeat as needed or as directed by a doctor [bullet] discard mixture after each use”.

(ii) *For topical products intended for direct application.* The labeling states “apply as needed”.

(3) *For products containing sodium bicarbonate identified in § 347.10(o).* The labeling states “[bullet] adults and children 2 years of age and over:”

(i) The labeling states “For use as a paste: [bullet] add enough water to the sodium bicarbonate to form a paste [bullet] apply to the affected area of the skin as needed, or as directed by a doctor”.

(ii) The labeling states “For use as a soak in a bath: [bullet] dissolve 1 to 2 cupfuls in a tub of warm water [bullet] soak for 10 to 30 minutes as

needed, or as directed by a doctor [bullet] pat dry (do not rub) to keep a thin layer on the skin”.

(iii) The labeling states “For use as a compress or wet dressing: [bullet] add sodium bicarbonate to water to make a mixture in a container [bullet] soak a clean, soft cloth in the mixture [bullet] apply cloth loosely to affected area for 15 to 30 minutes [bullet] repeat as needed or as directed by a doctor [bullet] discard mixture after each use”.

(iv) Any of the directions in paragraphs (d)(3)(i), (d)(3)(ii), or (d)(3)(iii) of this section shall be followed by the statement: “[bullet] children under 2 years: ask a doctor”.

(4) *For products containing aluminum hydroxide gel identified in § 347.10(b).* The labeling states “[bullet] children under 6 months: ask a doctor”.

(5) *For products containing glycerin identified in § 347.10(h).* The labeling states “[bullet] children under 6 months: ask a doctor”.

(6) *For products containing zinc acetate identified in § 347.10(s).* The labeling states “[bullet] children under 2 years: ask a doctor”.

(e) *Products formulated and labeled as a lip protectant and that meet the criteria established in § 201.66(d)(10) of this chapter.* The title, headings, subheadings, and information described in § 201.66(c) of this chapter shall be printed in accordance with the following specifications:

(1) The labeling shall meet the requirements of § 201.66(c) of this chapter except that the title, headings, and information described in § 201.66(c)(1), (c)(3), (c)(6), and (c)(7) may be omitted, and the headings, subheadings, and information described in § 201.66(c)(2), (c)(4), and (c)(5) may be presented as follows:

(i) The active ingredients (§ 201.66(c)(2) of this chapter) shall be listed in alphabetical order.

(ii) The heading and the indication required by § 201.66(c)(4) may be limited to: “Use [in bold type] helps protect” (which may be followed by “and relieve”) “chapped lips”.

(iii) The “external use only” warning in § 347.50(c)(1) and in § 201.66(c)(5)(i) of this chapter may be omitted. The warnings in § 347.50(c)(2) and (c)(4) are not required and the warning in § 347.50(c)(3) may be revised to read “Stop use and ask a doctor if condition lasts more than 7 days.”

(iv) The subheadings in § 201.66(c)(5)(iii) through (c)(5)(vi) of this chapter may be omitted, provided the information after the heading “Warning” contains the warning in § 347.50(e)(1)(iii).

(v) The warnings in § 201.66(c)(5)(x) of this chapter may be omitted.

(2) The labeling shall be printed in accordance with the requirements of § 201.66(d) of this chapter except that any requirements related to § 201.66(c)(1), (c)(3), (c)(6), and (c)(7), and the horizontal barlines and hairlines described in § 201.66(d)(8), may be omitted.

(f) *Products containing only cocoa butter, petrolatum, or white petrolatum identified in § 347.10(d), (m), and (r), singly or in combination with each other, and marketed other than as a lip protectant.* (1) The labeling shall meet the requirements of § 201.66(c) of this chapter except that the headings and information described in § 201.66(c)(3) and (c)(7) may be omitted, and the headings, subheadings, and information described in § 201.66(c)(2), (c)(4), and (c)(5) may be presented as follows:

(i) The active ingredients (§ 201.66(c)(2) of this chapter) shall be listed in alphabetical order.

(ii) The heading and the indication required by § 201.66(c)(4) of this chapter may be limited to “Use [in bold type] helps protect minor cuts and burns” or “Use [in bold type] helps protect chapped skin” or “Use [in bold type] helps protect minor cuts and burns and chapped skin”.

(iii) The warning in § 347.50(c)(3) may be revised to read “See a doctor if condition lasts more than 7 days.”

(iv) The subheadings in § 201.66(c)(5)(iv) through (c)(5)(vii) of this chapter may be omitted, provided the information after the heading “Warnings” contains the warnings in § 347.50(c)(2), (c)(4), and (f)(1)(iii).

(2) The labeling shall be printed in accordance with the requirements of § 201.66(d) of this chapter except that any requirements related to § 201.66(c)(3) and (c)(7) may be omitted.

§ 347.52 Labeling of astringent drug products.

(a) *Statement of identity.* The labeling of the product contains the established name of the drug, if any, and identifies the product as an “astringent.”

(b) *Indications.* The labeling of the product states, under the heading “Uses” any of the phrases listed in this paragraph (b), as appropriate. Other truthful and nonmisleading statements describing only the indications for use that have been established and listed in this paragraph (b) may also be used, as provided in § 330.1(c)(2) of this chapter, subject to the provisions of section 502 of the Federal Food, Drug, and Cosmetic Act (the act) relating to misbranding and the prohibition of section 301(d) of the act against the introduction or delivery for introduction into interstate commerce of unapproved new drugs in violation of section 505(a) of the act.

(1) *For products containing aluminum acetate identified in § 347.12(a).*
 “For temporary relief of minor skin irritations due to: [select one or more of

the following: 'poison ivy,' 'poison oak,' 'poison sumac,' 'insect bites,' 'athlete's foot,' or 'rashes caused by soaps, detergents, cosmetics, or jewelry']."

(2) *For products containing aluminum sulfate identified in § 347.12(b) for use as a styptic pencil.* "Stops bleeding caused by minor surface cuts and abrasions as may occur during shaving."

(3) *For products containing witch hazel identified in § 347.12(c).* "Relieves minor skin irritations due to: [select one or more of the following: 'insect bites,' 'minor cuts,' or 'minor scrapes']." [If more than one condition is used, each is preceded by a bullet.]

(c) *Warnings.* The labeling of the product contains the following warnings under the heading "Warnings":

(1) "For external use only. Avoid contact with the eyes."

(2) *For products containing aluminum acetate identified in § 347.12(a) or witch hazel identified in § 347.12(c).* "If condition worsens or symptoms persist for more than 7 days, discontinue use of the product and consult a" [select one of the following: 'physician' or 'doctor']."

(3) *For products containing aluminum acetate identified in § 347.12(a) used as a compress or wet dressing.* "Do not cover compress or wet dressing with plastic to prevent evaporation."

(d) *Directions.* The labeling of the product contains the following information under the heading "Directions":

(1) *For products containing aluminum acetate identified in § 347.12(a)—*

(i) *For products used as a soak.* "For use as a soak: Soak affected area in the solution for 15 to 30 minutes. Discard solution after each use. Repeat 3 times a day."

(ii) *For products used as a compress or wet dressing.* "For use as a compress or wet dressing: saturate a clean, soft white cloth (such as a diaper

or torn sheet) in the solution, gently squeeze, and apply loosely to the affected area. Saturate the cloth in the solution every 15 to 30 minutes and apply to the affected area. Discard solution after each use. Repeat as often as necessary.”

(2) *For products containing aluminum sulfate identified in § 347.12(b) for use as a styptic pencil.* “Moisten tip of pencil with water and apply to the affected area. Dry pencil after use.”

(3) *For products containing witch hazel identified in § 347.12(c).* “Apply to the affected area as often as necessary.”

§ 347.60 Labeling of permitted combinations of active ingredients.

The statement of identity, indications, warnings, and directions for use, respectively, applicable to each ingredient in the product may be combined to eliminate duplicative words or phrases so that the resulting information is clear and understandable.

(a) *Statement of identity.* For a combination drug product that has an established name, the labeling of the product states the established name of the combination drug product, followed by the statement of identity for each ingredient in the combination, as established in the statement of identity sections of the applicable OTC drug monographs. For a combination drug product that does not have an established name, the labeling of the product states the statement of identity for each ingredient in the combination, as established in the statement of identity sections of the applicable OTC drug monographs.

(b) *Indications.* The labeling of the product states, under the heading “Uses,” the indication(s) for each ingredient in the combination as established in the indications sections of the applicable OTC drug monographs, unless otherwise stated in this paragraph (b). Other truthful and nonmisleading statements, describing only the indications for use that have been established

in the applicable OTC drug monographs or listed in this paragraph (b) may also be used, as provided in § 330.1(c)(2) of this chapter, subject to the provisions of section 502 of the Federal Food, Drug, and Cosmetic Act (the act) relating to misbranding and the prohibition in section 301(d) of the act against the introduction or delivery for introduction into interstate commerce of unapproved new drugs in violation of section 505(a) of the act. In addition to the required information identified in this paragraph (b), the labeling of the product may contain any of the “other allowable statements” that are identified in the applicable monographs, provided such statements are neither placed in direct conjunction with information required to appear in the labeling nor occupy labeling space with greater prominence or conspicuousness than the required information.

(1) *Combinations of skin protectant and external analgesic active ingredients in § 347.20(b).* In addition to any or all of the indications for skin protectant drug products in § 347.50(b)(1), any or all of the allowable indications for external analgesic drug products may be used if the product is labeled for concurrent symptoms.

(2) *Combinations of skin protectant and first aid antiseptic active ingredients in § 347.20(c).* In addition to any or all of the indications for skin protectant drug products in § 347.50(b)(1), the required indications for first aid antiseptic drug products should be used.

(3) *Combinations of skin protectant and sunscreen active ingredients in § 347.20(d).* In addition to any or all of the indications for skin protectant drug products in § 347.50(b)(2)(i), the required indications for sunscreen drug products should be used and any or all of the additional indications for sunscreen drug products may be used.

(c) *Warnings.* The labeling of the product states, under the heading “Warnings,” the warning(s) for each ingredient in the combination, as established in the warnings section of the applicable OTC drug monographs unless otherwise stated in this paragraph (c).

(1) *For combinations containing a skin protectant and a sunscreen identified in §§ 347.20(d) and 352.20(b).* The warnings for sunscreen drug products in § 352.60(c) of this chapter are used.

(2) [Reserved]

(d) *Directions.* The labeling of the product states, under the heading “Directions,” directions that conform to the directions established for each ingredient in the directions sections of the applicable OTC drug monographs, unless otherwise stated in this paragraph (d). When the time intervals or age limitations for administration of the individual ingredients differ, the directions for the combination product may not contain any dosage that exceeds those established for any individual ingredient in the applicable OTC drug monograph(s), and may not provide for use by any age group lower than the highest minimum age limit established for any individual ingredient.

(1) *For combinations containing a skin protectant and a sunscreen identified in §§ 347.20(d) and 352.20(b).* The directions for sunscreen drug products in § 352.60(d) of this chapter are used.

(2) [Reserved]

PART 352—SUNSCREEN DRUG PRODUCTS FOR OVER-THE-COUNTER HUMAN USE

9. The authority citation for 21 CFR part 352 continues to read as follows:

Authority: 21 U.S.C. 321, 351, 352, 353, 355, 360, 371.

10. The stay of 21 CFR part 352 published at 66 FR 67485, December 31, 2001, is lifted.

11. Section 352.20 is amended by adding paragraph (b) to read as follows:

§ 352.20 Permitted combinations of active ingredients.

* * * * *

(b) *Combinations of sunscreen and skin protectant active ingredients.* Any single sunscreen active ingredient or any permitted combination of sunscreen active ingredients when used in the concentrations established for each ingredient in § 352.10 may be combined with one or more skin protectant active ingredients identified in § 347.10(a), (d), (e), (g), (h), (i), (k), (l), (m), and (r) of this chapter. The concentration of each sunscreen active ingredient must be sufficient to contribute a minimum SPF of not less than 2 to the finished product. The finished product must have a minimum SPF of not less than the number of sunscreen active ingredients used in the combination multiplied by 2, and the product must be labeled according to § 352.60.

12. Section 352.52 is amended by revising the heading in paragraphs (c)(2) and (d)(4) and by revising paragraphs (f)(1)(ii) and (f)(1)(vi) to read as follows:

§ 352.52 Labeling of sunscreen drug products.

* * * * *

(c) * * *

(2) *For products containing any ingredient identified in § 352.10 marketed as a lip protectant or lipstick.* * * *

(d) * * *

(4) *For products marketed as a lip protectant or lipstick.* * * *

* * * * *

(f) * * *

(1) * * *

(ii) The heading and the indication required by § 201.66(c)(4) of this chapter may be limited to: “Use [in bold type] helps protect against sunburn.” For a lip protectant product, the heading and the indication required by § 201.66(c)(4) may be limited to: “Use [in bold type] helps protect against sunburn and chapped lips.”

* * * *

(vi) For a lip protectant product or lipstick, the warnings “Keep out of eyes” in § 352.52(f)(1)(iv) and “Keep out of reach of children” in § 352.52(f)(1)(v) and the directions in § 352.52(d) may be omitted.

* * * *

13. Section 352.60 is amended by revising paragraphs (b)(2), (c), and (d) to read as follows:

§ 352.60 Labeling of permitted combinations of active ingredients.

* * * *

(b) * * *

(2) For permitted combinations containing a sunscreen and a skin protectant identified in § 352.20(b), any or all of the applicable indications for sunscreens in § 352.52(b) and the indication for skin protectants in § 347.50(b)(2)(i) of this chapter should be used. For products marketed as a lip protectant, the indication in § 352.52(f)(1)(ii) should be used.

(c) *Warnings.* The labeling of the product states, under the heading “Warnings,” the warning(s) for each ingredient in the combination, as established in the warnings section of the applicable OTC drug monographs, except that the warning for skin protectants in § 347.50(c)(3) of this chapter is not required for permitted combinations containing a sunscreen and a skin protectant identified in § 352.20(b). For products marketed as a lip protectant

or lipstick, § 352.52(f)(1)(iii), (f)(1)(iv) (except “Keep out of eyes,” which may be omitted), and (f)(1)(vi) apply.

(d) *Directions*. The labeling of the product states, under the heading “directions,” directions that conform to the directions established for each ingredient in the directions sections of the applicable OTC drug monographs, unless otherwise stated in this paragraph. When the time intervals or age limitations for administration of the individual ingredients differ, the directions for the combination product may not contain any dosage that exceeds those established for any individual ingredient in the applicable OTC drug monograph(s), and may not provide for use by any age group lower than the highest minimum age limit established for any individual ingredient. For permitted combinations containing a sunscreen and a skin protectant identified in § 352.20(b), the directions for sunscreens in § 352.52(d) should be used. For products marketed as a lip protectant or lipstick, § 352.52(d)(4) applies.

14. Part 352 is stayed until further notice.

Dated: May 16, 2003.

Jeffrey Shuren,

Assistant Commissioner for Policy.

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